Louisiana Clinical and Translational Science Center (LA CaTS)

Roadmap Scholar Program Application

Title: Role of IL-22 BP in Sinopulmonary Infection and Colonization with *Staphylococcus Aureus*

Applicant:

Jane Doe, MD

Tulane University
Department of Medicine
Section of Pulmonary Diseases, Critical Care and Environmental Medicine
1430 Tulane Avenue
#8509
New Orleans, LA 70112
Email: exampleemail@tulane.edu

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted]

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Assistant Professor of Medicine, Tulane University School of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Vanderbilt University, Nashville, TN	B.S.	05/2003	Neuroscience
George Washington University School of Medicine, Washington, DC	M.D.	05/2010	Medicine
Louisiana University Health Sciences Center – New Orleans, New Orleans, LA		05/2014	Combined Internal Medicine and Pediatrics Residency
University of California, San Diego (UCSD), San Diego, CA		06/2018	Pulmonary Critical Care Fellowship

A. Personal Statement

A predominant feature of the clinical syndrome of cystic fibrosis and non-cystic fibrosis bronchiectasis is chronic infections with key pathogens leading to decreased lung function and lowered survival rates. Through the use of both humanized transgenic mice and human samples, the goal of my proposed research is to investigate the role of IL-22 binding protein (IL-22 BP) in promoting sinopulmonary infection and colonization specifically with the pathogen *Staphylococcus aureus*. Data obtained from the proposed project will serve as preliminary pilot and feasibility data for a career development award investigating novel therapeutic targets and/or interventions aimed at decreasing the rate of chronic sinopulmonary infections with *S. aureus*. My background in basic and translational immunology research obtained during my completion of an NIH Post-baccalaureate Intramural Training Award fellowship and during my sub-specialty training at University of California, San Diego (UCSD) on an institutional T32 award, combined with my strong mentorship team, make me an excellent candidate for the Roadmap Scholars Program.

As a new junior faculty member with a strong background in basic bench and translational research, as evidenced by 15 original research publications in peer-reviewed journals, and with my clinical expertise in cystic fibrosis and non-cystic fibrosis bronchiectasis as the Associate Director of the Tulane Adult Cystic Fibrosis Program, I am in a prime position to take research from bench to bedside and from bedside to bench. During my fellowship training, support from an NIH-T32 training grant allowed me to develop a background in neutrophil biology. Through one-on-one teaching from expert mentors, attendance at international pulmonary conferences, and independent study, I now aim to study the role of the important cytokine IL-22 and IL-22 BP. I am fortunate to have the support from mentors within the Section of Pulmonary Diseases, Critical Care and Environmental Medicine and the Department of Microbiology and Immunology, as this allows me to take a multidisciplinary

approach to my area of interest. At this early stage in my career, I also recognize my need for further translational training in study design, epidemiologic principles and biostatistical methods that I will obtain through completion of the MSCR program during the time period of this award. I have the background training, clinical expertise and exposure, and a strong motivation to ensure that my proposed project is successful.

The academic environment at Tulane University provides an ideal multi-disciplinary team of mentors and a network of collaborators. Dr. [redacted] is my primary mentor and is an international leader in lung immunology and the Director of the Tulane School of Medicine's Center for Translational Research in Infection and Inflammation. My additional mentors include Dr. [redacted], Chair of the Department of Microbiology and Immunology and recognized expert in the study of IL-22, and Dr. [redacted], Chief of Pulmonary Diseases, Critical Care and Environmental Medicine and an expert in translational lung study development. My mentorship committee has a long track record of significant contributions to science and in the successful development of trainees.

Participation in the LA CaTS Roadmap Scholar Program will combine advanced training in translational research methods along with the robust mentorship structure needed to ensure my successful transition as a junior faculty member. This mentored award will equip me with a distinct skillset that will advance me towards my long-term career goal of becoming an expert independent clinician-scientist investigating innate host response in chronic lung infection.

B. Positions and Honors

Positions

August 2018 – Present	Assistant Professor, Department of Medicine Associate Director, Tulane Adult Cystic Fibrosis Program
August 2018 – Present	Staff Physician, Southeastern Louisiana Veterans HealthCare System

Other Experience and Professional Memberships

2004-2005	Chairperson, NIH Post-Baccalaureate IRTA Fellowship Committee
2013-2014	President, LSUHSC House Staff Association
2013-2014	Member, LSUHSC Graduate Medical Education Committee
2015-2017	Member, University of California, San Diego Graduate Medical Education Committee
2015-present	Member, American Thoracic Society
2015-present	Member, American College of Chest Physicians
2018-present	Member, American Thoracic Society Training Committee
2018-present	Co-Chair, American Thoracic Society Training Committee, Career Development Core Training (CDCT) Sub-committee
2018-present	Member, American Thoracic Society Allergy, Immunology, and Inflammation Assembly

Honors

2003-2005	National Institutes of Health Intramural Research Training Award (IRTA) Fellowship
2006	Recipient of the National Eye Institute Travel Grant
2006	Recipient of the Donald H. Glew Memorial Award – George Washington University Medical Center Research Day
2006	George Washington University Medical Center Summer Scholarship Recipient
2011 – 2013	Aesculapian Society Resident Excellence in Teaching Award Nominee, Louisiana State University
2014	Recipient of the LSU Medicine-Pediatrics Resident of the Year Award
2017-2018	Chief Fellow, Pulmonary, Critical Care and Sleep Medicine, University of California, San Diego
2017-2018	Appointment to the University of California, San Diego Division of Pulmonary, Critical Care, and Sleep Medicine NIH T32 Training Grant

C. Contribution to Science

1. Immunology and Age-Related Macular Degeneration: One of my early interests in basic and translational science research was studying the genetic factors that contribute to the development of age-related macular degeneration under the mentorship of Dr. Chi-Chao Chan at the National Eye Institute. I received a National Institutes of Health post-baccalaureate Intramural Research Training Award (IRTA) to support my studies. The targets for the studies I was involved in were primarily genes critical in host response, chemotaxis, and inflammation. During this time, I learned several basic techniques and contributed to the development of a murine *Ccl2/Cx3cr1* deficiency model that mimics the retinal lesions seen in age-related macular degeneration. Data from this work led to over 20 abstract presentations (both oral and poster) at international meetings and eight publications in peer-reviewed journals, including FASEB and PNAS.

- [redacted], Tuo J, Chew EY, Csaky KG, Chan CC: Analysis of Hemicentin-1, hOgg1, and E-selectin in Age-Related Macular Degeneration. Trans Am Ophthalmol Soc 2005; Dec 103; 37-45. PMID: 17057786
- Tuo J, Ning B, [redacted] Ross RI, Reed GF, Shen D. Jiao X, Zhou M, Chew EY, Kadlubar FF, Chan CC. Synergic effect of polymorphisms in *ERCC6* 5' flanking region and *complement factor H* on age-related macular degeneration predisposition. Proc Natl Acad Sci 2006; Jun 103 (24): 9256-9261. PMID: 16754848
- [redacted], Shen D, Chew EY, Ning B, Csaky KG, Green WR, Chan CC, Tou J. An apolipoprotein E variant may protect against age-related macular degeneration through cytokine regulation. Environ Mol Mutagen 2006; 47 (8): 594-602. PMID: 16823865
- Tuo J, [redacted] Zhou M, Shen D, Ross RJ, Rosenberg KI, Cameron DJ, Yin C, Kowalak JA, Zhuang Z, Zhang K, Chan CC: Murine *Ccl2/Cx3cr1* deficiency results in retinal lesions mimicking human age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2007 Aug;48(8):3827-3836. PMID: 1765275

2. Outcomes in Systemic Sclerosis related Pulmonary Arterial Hypertension: As a resident physician, I developed a keen interest in lung disease. As a 4th year resident, I had the opportunity to study the association between oral therapy selection and outcomes in a multi-center collaborative project along with Dr. Lammi, a former LA CaTS Roadmap Scholar. This was an important learning experience in statistical data analysis.

- Lammi MR, Mathai SC, Saketkoo LA, Domsic RT, [redacted], Steen VD; PHAROS Investigators. Association between Initial Oral Therapy and Outcomes in Systemic Sclerosis related Pulmonary Arterial Hypertension: Observations from PHAROS. Arthritis Rheumatol. 2016 MAR: 68 (3): 740-8. PMID: 26479414

3. Clinical Management in Cystic Fibrosis: Being board certified in both Internal Medicine and Pediatrics, I am clinically interested in transitional pediatric to adult chronic lung disease including cystic fibrosis. Airway inflammation and bacterial virulence are clinically extremely important factors in this chronic clinical syndrome. I have been working to grow into a clinical expert in this field and have given two oral presentations at the primary national conference in this area. Since joining the Tulane University Adult Cystic Fibrosis Program as Associate Director, I am also now the sub-PI for two current on-going Vertex trials

- [redacted]. The Microbiome and Cystic Fibrosis. Adult Fellows Grand Rounds. NACFC 2016. Orlando, FL
- [redacted]. Inhaled Sodium Bicarbonate Therapy in Cystic Fibrosis. Adult Fellows Grand Rounds. NACFC 2017. Indianapolis, IN
- On-going Trials as Sub-Principal Investigator
    - Study title: VX17-445-102: A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX 445 Combination Therapy in Subjects With Cystic Fibrosis Who Are Heterozygous for the F508del Mutation and a Minimal Function Mutation (F/MF)
    - Study title: VX17-445-105: A Phase 3, Open-label Study Evaluating the Long term Safety and Efficacy of VX 445 Combination Therapy in Subjects With Cystic Fibrosis Who Are Homozygous or Heterozygous for the F508del Mutation

4. **Neutrophil Biology and Innate Host Response to E-cigarettes Exposure:** Neutrophils are first in the line of innate host responses to insults within the lung. During my sub-specialty fellowship in Pulmonary and Critical Care Medicine, I was appointed to our NIH funded institutional T-32 training grant. During this time, under the

mentorship of Dr. Laura Crotty Alexander, my research in this area sought to elucidate the impact of E-cigarette vapor exposure on neutrophil function both *in vitro* and *ex vivo*. I conducted experiments and delivered both oral and poster research abstract presentations at the international American Thoracic Society (ATS) meeting. Through this work, I learned several bench techniques as well as gained valuable knowledge in human study design. Additionally, we are currently completing several manuscripts, two of which have been submitted to peer-reviewed journals.

- [redacted], Chuki D, El-Hajjaoui T, Crotty Alexander LE. Electronic Cigarette Use Patterns in San Diego County. RAPiD Poster Discussion. Abstract #A6247, 2018, San Diego, CA
- [redacted], Corriden R, Meier A, Crotty Alexander LE. Electronic Cigarette Vapor Extract (EVE) Impairs Neutrophil Chemotaxis, ROS production and NET Formation. Abstract #A3564, 2018, San Diego, CA
- [redacted], Corriden R, Chien J, Crotty Alexander LE. Electronic Cigarette Use Alters RNA Expression in E-cigarette Users. Abstract #A3562, 2018, San Diego, CA
- Moshensky A, Hepokoski M, [redacted], Nguyen N, Crotty Alexander LE. Chronic Inhalation of Electronic (e)-cigarette Vapor Increases Susceptibility to Acute Lung Injury. Abstract #A3568, 2018, San Diego, CA

5. Clinical Case Reports and Medical Education: My primary career goal is to become an independent physician-scientist. However, I remain a passionate clinician and have taken opportunities to present and publish interesting cases in order to share ideas and experiences in the management of unique or complicated cases. Participation in medical education is vital to recruiting the best and brightest physicians into academic medicine. As a Chief Pulmonary Critical Care Fellow and now Assistant Professor, I have been involved with multiple medical education initiatives involving fellows, residents and medical students and have presented 7 case reports as first author at meetings. As a pulmonary fellow, I became involved with education initiatives nationally through the ATS and I am now a member of the ATS Training Committee. I also co-authored the Infectious Disease Chapter in the recently published ATS critical care board review.

- [redacted], Yi ES, Wang H-Y, Pretorius G, Auger WR, Lin GY. A Case of Inflammatory Pseudotumor Presenting as Chronic Thromboembolic Disease: a Rare and Controversial Entity. American Thoracic Society Abstract # A67. 2016. San Francisco, CA
- [redacted] Pretorius V, Fernandes TM. An Uncommon Cause for a Common Complaint: Dyspnea on Exertion Caused by a Double Aortic Arch. Abstract #A6751, 2018, San Diego, CA
- Hepokoski ML, Bellinghausen AL, [redacted] Malhotra A. Recommended Reading from University of California, San Diego Division of Pulmonary and Critical Care Medicine Fellows. Am J Respir Crit Care Med. 2018 Aug 28. DOI: 10.1164/rccm.201712-2573RR. [Epub ahead of print]. PMID: 30153048
- [redacted], et al. (2018). Infectious Disease. In S Pasnick, et al (Eds.), *ATS Review for the Critical Care Boards* (94-193). New York, NY: American Thoracic Society.

URL to published peer-review articles on My Bibliography:

https://www.ncbi.nlm.nih.gov/sites/myncbi/1XGse8OBX1zIeg/bibliography/[redacted]/public/?sort=date&direction=ascending

D. Additional Information: Research Support

On-going Research Support

None Currently

Completed Research Support

July 1, 2017-June 30, 2018

Appointment to the University of California, San Diego Division of Pulmonary, Critical Care, and Sleep Medicine NIH T32 Training Grant

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted] Primary Mentor: Last name, First name

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor of Medicine and Pediatrics, Director, Center for Translational Research in Infection and Inflammation

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Ursinus College, Collegeville, PA	BS	1981	Physics
University of Maryland	MD	1985	Medicine
Louisiana State University Medical Center	Intern	1985-1986	Medicine/Pediatrics
Louisiana State University Medical Center	Residency	1986-1989	Medicine/Pediatrics
Tulane Univ. Medical Center, New Orleans, LA	Fellowship	1989-1993	Pediatric Pulmonology
Louisiana State University Medical Center	Fellowship	1990-1993	Adult Pulmonary Medicine
Louisiana State University Medical Center	Research Fellowship	1991-1992	LSU Section of Pulmonary/Critical Care
Howard Hughes Medical Institute - Laboratory of Bruce Beutler, UT Southwestern, Dallas, TX	PostDoctoral Research Fellowship	1992-1993	Immunology/Genetics

Personal Statement. I have been continuously funded by the NIH for 20 years for work on lung/mucosal immunology. We identified IL-17 and IL-22, cytokines produced by T cells and innate lymphoid cells are critical to pulmonary host defense to extracellular bacteria. Moreover using conditional genetics we showed that the receptor for these cytokines are critical for mucosal immune responses in the gut and intestine, in part by regulating paneth cell development and sIgA transport. We went on to study the evolution of IL-17 family member cytokines and demonstrated that the two IL-17 family members that are expressed in T cells, IL-17A, and IL-17F co-evolved with Rag genes suggesting co-evolution with the ability to recombine the TCR and the host to make antigen specific memory responses. Based on this, we demonstrated that antigen specific memory Th17 cells can mediate clade specific immunity against enterobacteriaceae including multi-drug resistant Klebsiella pneumonia.

A major focus of my lab is understanding mucosal immunity to extracellular pathogens. To this end we have used RNAseq to decipher the role of IL-17R and Il-22Ra1 signaling control mucosal immunity in the lung and gut. Additionally we have found high levels of IL-22 binding protein (encoded by Il22ra2) in the sinus of subjects with cystic fibrosis.

Of relevance to this application I have trained many post-doctoral fellows as well as junior faculty toward career as independent investigators. I have served as the sponsor on 6 K08/K01 awards and I have mentored many junior faculty for their successful R01 applications.

Positions and Honors

Positions and Employment

Louisiana State University Medical Center, New Orleans, LA

1993-1997	Assistant Professor of Medicine and Pediatrics
1996-2011	Division Chief, Division of Pediatric Pulmonary/Critical Care
1997-2000	Associate Professor of Medicine and Pediatrics, Director LSU Gene Therapy Program
2000-2003	Professor of Medicine and Pediatrics, Director LSU Gene Therapy Program
2009-2011	Chair, Department of Genetics

University of Pittsburgh School of Medicine and Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA

2003-	Professor of Pediatrics, Division Chief Pediatric Pulmonology
2006-2009	Niels K. Jerne Professor of Pediatrics and Immunology
2009-2011	Adjunct Professor of Pediatrics and Immunology
2011-2017	Professor of Pediatrics and Medicine
2011-2017	Vice Chair for Translational Research
2011-2017	Director Richard King Mellon Foundation Institute for Pediatric Research
2012-2016	Interim T32 Program Director, Rheumatology

Tulane University School of Medicine, New Orleans, LA

2017-present	Professor of Medicine and Pediatrics, Director Center for Translational Research in Infection and Inflammation

Other

2002-2003	Member, Lung Biology Pathology Study Section
2003-2006	Member, Lung Cellular and Molecular Immunology Study Section
2006-2007	Chair, Lung Cellular and Molecular Immunology Study Section

Honors

1989	Winner of the American College of Chest Physicians Clinical Vignette Award
1991	Parker B. Francis Pulmonary Research Fellowship Award
1991	American Lung Association Pediatric Pulmonary Research Fellowship Award - declined
1994	First Place, Merck, Sharp, & Dohme Young Investigator Award
2004	Member, American Society of Clinical Investigation

Editorial Boards

2005-present	Section Editor, Journal of Immunology Consulting Editor, Journal of Clinical Investigation Advisory Editor, Journal of Experimental Medicine
2006-present	Consulting Editor, Journal of Clinical Investigations
2012-present	Associate Editor, American Journal of Respiratory Critical Care Medicine
2013-Present	Deputy Editor, Journal of Immunology

Contributions to Science:

1. Our lab identified the critical roles of IL-17 and IL-22 in gram negative pneumonia and demonstrated that antigen specific Th17 cells can provide serotype independent immunity to enterobacteriaceae. In addition we identified epithelial STAT3 and Reg3γ as key factor in lung immunity against MRSA.

1. Choi S-M., McAleer JP, Zheng M, Pociask DA, Kaplan MH, Qin S, Reinhart TA, [redacted] Innate Stat3-mediated induction of the antimicrobial protein, Reg3γ is required for host defense against MRSA pneumonia. J Exp Med. 2013 Mar 11;210(3):551-61. PMCID: PMC3600913
2. Chen K, McAleer JP, Lin Y, Paterson DL, Zheng M, Alcorn JF, Weaver CT, [redacted]. Th17 cells mediate clade-specific, serotype-independent mucosal immunity. Immunity. 2011 Dec 23;35(6):997-1009. PMCID: PMC3406408.
3. Aujla S, Chan YC, Zheng M, Fei M, Askew DJ, Pociask DA , Reinhart TA, McAllister F, Edeal J, Gaus K, Husain S, Kreindler JL, Dubin PJ, Pilewski JM, Myerburg MM, Mason CA, Iwakura Y, and [redacted]. IL-22 mediates mucosal host defense against gram negative bacterial pneumonia. Nat Med. 2008 Mar;14(3):275-81. PMCID: PMC2901867.

4. Chen K, Eddens T, Trevejo-Nunez G, Way EE, Elsegeiny W, Ricks DM, Garg AV, Erb CJ, Bo M, Wang T, Chen W, Lee JS, Gaffen SL, [redacted]. IL-17 Receptor Signaling in the Lung Epithelium Is Required for Mucosal Chemokine Gradients and Pulmonary Host Defense against K. pneumoniae. Cell Host Microbe. 2016 Nov 9;20(5):596-605. PMC5149406

2. Our lab has used RNAseq to assay inflammatory responses and ion transport pathways in the airway.

1. Chen K, Pociask DA, McAleer JP, Chan YR, Alcorn JF, Kreindler JL, Keyser MR, Shapiro SD, Houghton AM, [redacted], Zheng M IL-17RA is required for CCL2 expression, macrophage recruitment, and emphysema in response to cigarette smoke. PLoS One. 2011;6(5):e20333. doi: 10.1371/journal.pone.0020333. PMCID: PMC3103542
2. Adams KM, Abraham V, Spielman D, [redacted], Rubenstein RC, Conner GE, Cohen NA, Kreindler JL. IL-17A induces Pendrin expression and chloride-bicarbonate exchange in human bronchial epithelial cells. PLoS One. 2014 Aug 20;9(8):e103263. doi: 10.1371/journal.pone.0103263. PMCID: PMC4139276
3. Ray M, Horne W, McAleer JP, Ricks DM, Kreindler JL, Fitzsimons MS, Chan PP, Trevejo-Nunez G, Chen K, Fajt M, Chen W, Ray A, Wenzel S, and [redacted]. RNA-seq in Pulmonary Medicine – how much is enough? Am. J. Resp. Crit. Care, 2015. PMCID: PMC4584249.
4. Chen K, Campfield BT, Wenzel SE, McAleer JP, Kreindler JL, Kurland G, Gopal R, Wang T, Chen W, Eddens T, Quinn KM, Myerburg MM, Horne WT, Lora JM, Albrecht BK, Pilewski JM, [redacted]. Antiinflammatory effects of bromodomain and extraterminal domain inhibition in cystic fibrosis lung inflammation. JCI Insight. 2016 Jul 21;1(11). pii: e87168. PMCID: PMC4978187.

3. We have pioneered studies in the CD4+ T-cell and B-cell requirements for control of pneumocystis colonization was well as pioneered the use of novel proteomic strategies for antigen discovery that can be used for vaccines, therapeutic or diagnostics.

1. Elsegeiny W, Zheng M, Eddens T, Gallo RL, Dai G, Trevejo-Nunez G, Castillo P, Kracinovsky K, Cleveland H, Horne W, Franks J, Pociask D, Pilarski M, Alcorn JF, Chen K, [redacted]. Murine models of Pneumocystis infection recapitulate human primary immune disorders. JCI Insight. 2018 Jun 21;3(12). PMCID: in progress
2. Elsegeiny W, Eddens T, Chen K, [redacted]. Anti-CD20 and susceptibility to Pneumocystis Pneumonia. Infect Immun. 2015 Mar 2. pii: IAI.03099-14. PMCID: PMC4399075
3. Ricks D, Chen K, Zheng M, [redacted]. Dectin immunoadhesins and Pneumocystis pneumonia. Infect Immun. 2013 September; 81(9): 3451–3462. PMCID: PMC3754224.
4. Zheng M, Cai Y, Eddens T, Ricks DM, [redacted]. Novel Pneumocystis antigen discovery using fungal surface proteomics. Infect Immun.(in press). PMCID: PMC4019171

4. We have identified key roles of IL-17 and IL-22 in regulating the gut microbiota as well as regulating immunity to extracellular pathogens.

1. Trevejo-Nunez G, Chen K, Dufour JP, Bagby GJ, Horne WT, Nelson S, [redacted].
Ethanol Impairs Mucosal Immunity Against Streptococcus pneumoniae Infection by Disrupting IL-17 Gene Expression.Infect Immun. 2015 Mar 9. pii: IAI.02869-14 PMCID: in process.
3. Kumar P, Monin L, Castillo P, Elsegeiny W, Horne W, Eddens T, Vikram A, Good M, Schoenborn AA, Bibby K, Montelaro RC, Metzger DW, Gulati AS, and [redacted]. Intestinal interleukin-17 receptor signaling mediates reciprocal control of the gut microbiota and autoimmune inflammation. Immunity, 2016 Mar 15;44(3):659-71. PMCID: PMC4794750
4. Ectopic colonization of oral bacteria in the intestine drives TH1 cell induction and inflammation. Atarashi K, Suda W, Luo C, Kawaguchi T, Motoo I, Narushima S, Kiguchi Y, Yasuma K, Watanabe E, Tanoue T, Thaiss CA, Sato M, Toyooka K, Said HS, Yamagami H, Rice SA, Gevers D, Johnson RC, Segre JA, Chen K, [redacted] Elinav E, Morita H, Xavier RJ, Hattori M, Honda K. Science. 2017 Oct 20;358(6361):359-365.

Complete List of Published Work in PubMed:

http://www.ncbi.nlm.nih.gov/pubmed/?term=[redacted]

C. Research Support

Ongoing Research Support

R35HL139930-01 ([redacted]) 2/1/18-1/31/25 6.0 cal. months
NIH/NHLBI

CD4+ T-cell Immunity in the Lung

Pneumonia remains the #1 killer of children in the world and is a leading cause of morbidity and mortality in children in the US and the #8 cause of mortality in adults. The research prosed under this R35 will shed new light on pulmonary host defenses that can be exploited to reduce the global burden of pneumonia mortality and morbidity.

7R01 AI 120033-03 ([redacted]) 2/1/2016 – 1/31/2021 1.40 cal. months
NIH/NIAID $162,817
Improved Therapeutics and Diagnostics for Pneumocystis Pneumonia
This grant will identify novel targets to improve treatment outcomes as well as improve diagnostics for this pneumonia in patients lacking CD4+ T-cell immunity such as advanced AIDS.

7R21 AI 121815 -03 ([redacted]) 4/1/2016 – 3/31/2019 1.2 cal. months
NIH/NIAID $107,032
Generation of Novel Human Monoclonals for Lung Disease
Cystic Fibrosis is the most common lethal genetic disease in the US and is characterized by chronic infection inflammation in the airway. We have identified an important role of the immune system in controlling the infection in these patients and this proposal will try to develop novel therapies for lung infections based on this.

P01 AI 106684 (Ray, contact PI) (PI. RNAseq Core) 4/1/2015 – 3/31/2020 1.20 cal. months
University of Pittsburgh (NIH/NIAID) $160,000
Immune Airway-Epithelial Interactions in Steroid-Refractory Severe Asthma
The purpose of this proposal is to establish a new paradigm for severe asthma based on which novel therapeutics could be developed in the future using cutting edge immunological, cellular and RNA sequencing techniques.

5U19AG055373 (Deng, Contact PI) 9/15/2017-3/31/2022 0.6 cal. months

TRANS-OMICS INTEGRATION OF MULTI-OMICS STUDIES FOR MALE OSTEOPOROSIS. Dr [redacted] provides expertise on RNAseq for this project.

Novartis ([redacted]) 7/1/18-6/30/19 .12 cal. months

Exploring antibody-mediated B-cell depletion and the impact on Pneumocystis pneumonia infection in mice. This project examines the effect of anti-CD20 and fungal T-cell priming in the lung.

Completed Research Support (within the last 3 years)

R01-HL061271 [redacted] (PI) 6/01/2009-4/30/2015
Non-CD4 host Defense against P. carinii Pneumonia
The long-term goal is to test the hypothesis that bone-marrow derived DCs, genetically engineered to express CD40 ligand can result in effective vaccination and protection against PC in the absence of CD4+ T-cells.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted] Secondary Mentor: Last name, First name

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor and Chair

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Louisiana, Monroe, LA	BS	05/1995	Chemistry
Louisiana State University Health Sciences Center	MS	12/1998	Microbiology/Immunology
Louisiana State University Health Sciences Center	Ph.D.	12/2000	Microbiology/Immunology
Louisiana State University Health Sciences Center	Post-doc	06/2003	Pulmonary Immunology

A. Personal Statement

The [redacted] Laboratory initiated research in fungal asthma in 2010 and reported in 2012 that pathways critical for host defense against fungal pathogens, namely Dectin-1 mediated fungal beta-glucan recognition and IL-22 induction, function in an immunopathogenic capacity during allergic fungal asthma (J Immunol 189:3653-60, 2012). Pursuant to this, we reached out to investigators at Wake Forest University who were part of the NHLBI-supported Severe Asthma Research Program (SARP), initially to examine SNPs in Dectin-1 and IL-22. Since this time, we have actively collaborated with the Wake Forest asthma group and have characterized clinical differences in human asthmatics that were sensitized to fungi and conducted Luminex®-based biomarker assessments of BAL fluid and sputum. These analyses identified multiple mediators and pathways that we began to pursue in our experimental fungal asthma model, which is starting to bear fruit in terms of publications: (i) Luminex® sputum analysis of severe asthmatics – Clin Exp Allergy 48:787-797 (2018), (ii) acidic mammalian chitinase in fungal asthma – Infect Immun 86:e00944-17 (2018) and (iii)) Luminex® BAL fluid analysis of severe asthmatics and IL-7 in fungal asthma – Mucosal Immunol 11:1352-1362 (2018). We also have additional manuscripts under review (IL-1R and IL-1RA in fungal asthma, J Allergy Clin Immunol) or in preparation (TRAIL in human asthma, BRP-39 in experimental fungal asthma and CX3CL1 in experimental fungal asthma).

B. Positions and Honors

Positions

07/2003-08/2004 Research Assistant Professor, Department of Pediatrics, University of Pittsburgh, Pittsburgh, PA
09/2004-06/2007 Assistant Professor, Department of Pediatrics, University of Pittsburgh, Pittsburgh, PA
07/2007-09/2009 Associate Professor, Department of Medicine, University of Alabama at Birmingham
10/2009-09/2012 Associate Professor (with tenure), Department of Medicine, University of Alabama at Birmingham
10/2012-02/2018 Professor (with tenure), Department of Medicine, University of Alabama at Birmingham
07/2015-02/2018 Assistant Dean for Research Administration, School of Medicine, University of Alabama at Birmingham
09/2015-02/2018 Inaugural Endowed Professor in Lung Immunology, Department of Medicine, University of Alabama at Birmingham
03/2018-present Professor and Chair, Department of Microbiology and Immunology, Tulane University

Honors/Awards (last 10 years):

2008 Editorial Board – *Infection and Immunity* (reappointed 2017 – 2019)
2008 Associate Editor – *The Journal of Immunology*
2009 Editorial Board – *The American Journal of Physiology - Lung Cellular and Molecular Physiology*
2009 Member, AIDS-associated Opportunistic Infections and Cancer (AOIC) study section, NIH CSR
2009 The Max Cooper Award for Research Excellence, Department of Medicine, UAB
2010 Section Editor – *The Journal of Immunology*
2011 Spotlight Article for Werner et al., *Infection and Immunity*, October 2011
2011 Editorial Board – *The American Journal of Physiology - Lung Cellular and Molecular Physiology*
2012 Spotlight Article for Gessner et al., *Infection and Immunity*, January 2012
2012 Section Editor – *The Journal of Immunology* (reappointed 2012 – 2014)
2012 Editorial Board – *PLoS ONE*
2013 American Heart Association – Lung Basic Science 2 Review Committee
2014 Elected Chair of the 2018 Gordon Research Conference – Biology of Acute Respiratory Infections
2015 Awarded the first Endowed Professorship in Lung Immunology, Department of Medicine, University of Alabama at Birmingham
2018 Chair, Gordon Research Conference – Biology of Acute Respiratory Infections
2018 Council of Scientific Advisors, Parker B. Francis Foundation
2018 Member, Immunity and Host Defense (IHD) study section, NIH CSR
2018 Review Editor – Fungal Pathogenesis, *Frontiers in Cellular and Infection Microbiology*
2018 Spotlight Article for Reeder et al., *Infection and Immunity*, October 2018

C. Contributions to Science

1. The fungal beta-glucan receptor Dectin-1

During my post-doctoral fellowship, I discovered that killing of *Pneumocystis carinii* by AMs involved a beta-glucan inhibitable receptor. Shortly thereafter, the Dectin-1 beta-glucan receptor was identified and we subsequently showed that Dectin-1 mediated both the killing function and proinflammatory response of AMs to *P. carinii*. This led to a long and fruitful collaboration between myself and Gordon Brown where we have reported roles for Dectin-1 in innate immunity against *P. carinii*, *C. albicans* and *A. fumigatus*. Notable findings in the latter included the discovery that beta-glucans in *A. fumigatus* were unmasked as the organism swelled and germinated, providing a "window" in which Dectin-1 could recognize the organism. We subsequently showed that Dectin-1 deficiency resulted in profound susceptibility to lung infection with *A. fumigatus* as a result of impaired AM inflammatory responses, impaired neutrophil recruitment to the lungs as well as impaired neutrophil oxidative killing.

a. [redacted] L. Marrero, S. Swain, A.G. Harmsen, M. Zheng, G.D. Brown, S. Gordon, J.E. Shellito and [redacted]. Alveolar macrophage-mediated killing of *Pneumocystis carinii* f. sp. muris involves pattern recognition by the Dectin-1 beta-glucan receptor. *Journal of Experimental Medicine* 198:1677-1688 (2003). **Cover article - December 1, 2003 Issue** PMCID:PMC2194130

b. [redacted] R. Rapaka, A. Metz, S.M. Pop, D.L. Williams, S. Gordon, [redacted] and G.D. Brown. The beta glucan receptor Dectin-1 recognizes specific morphologies of *Aspergillus fumigatus*. *PLoS Pathogens* 1:e42 (2005). **Cover article - December 2005 Issue**; **nominated to Faculty of 1000 Biology by June Kwon-Chung, Ph.D., NIAID/NIH – March 2006** PMCID:PMC1311140

c. Taylor, P.R., S.V. Tsoni, J.A. Willment, K.M. Dennehy, M. Rosas, H. Findon, K. Haynes, [redacted], M. Botto, S. Gordon and G.D. Brown. Dectin-1 is required for β-glucan recognition and control of fungal infection. *Nature Immunology* 8:31-38 (2007). **Cover article - January 2007 Issue** PMCID:PMC1888731

d. Werner, J., A.E. Metz, D. Horn, I. Faro-Trindade, T.R. Schoeb, M.M. Hewitt, L.M. Schwiebert, G.D. Brown and [redacted]. Requisite role for the Dectin-1 beta-glucan receptor in pulmonary defense against *Aspergillus fumigatus*. *Journal of Immunology* 182:4938-4946 (2009). ** In This Issue Highlight Article – April 15, 2009** PMCID:PMC3434356

2. Immunity against *Aspergillus fumigatus*.

For the last 15 years, my lab has primarily focused on host defense mechanisms against invasive fungal infection caused by *A. fumigatus*. This initially focused on Dectin-1 where we subsequently showed that Dectin-1 controls innate production of IL-17A and IL-22, both of which are required for *A. fumigatus* elimination.

a. Gessner, M.A., S. Doran, Z. Yu, C.W. Dunaway, S. Matalon and [redacted]. Chlorine gas exposure increases susceptibility to invasive lung fungal infection. *American Journal of Physiology – Lung Cellular and Molecular Physiology* 304:L765-73 (2013).

b. Lilly, L.M., M.P. Nelson, A.R. Burg, C.W. Dunaway and [redacted]. Eosinophil deficiency compromises lung defense against *Aspergillus fumigatus*. *Infection and Immunity* 82:1315-25 (2014).

c. Garth J.M., K.M. Reeder, M.S. Godwin, C W. Dunaway, J.P. Blackburn and [redacted] IL-33 signaling regulates innate IL-17A and IL-22 production via suppression of PGE2 during lung fungal infection. *Journal of Immunology* 199:2140-2148 (2017)

d. Reeder K.R., M.S. Godwin, J.M. Mackel, C.W. Dunaway, J.P. Blackburn, R.P. Patel and [redacted]. The role of common γ-chain cytokines in lung IL-22 regulation after acute exposure to *Aspergillus fumigatus*. *Infection and Immunity* 2018 Aug 13. pii: IAI.00157-18. ****Spotlight Article – Articles of Significant Interest Selected from This Issue by the Editors, October 2018 Issue****

3. <u>Severe asthma associated with fungal sensitization</u>

In addition to invasive infection, we have also become interested in the role *A. fumigatus* played in other lung diseases, namely cystic fibrosis (CF) and asthma. Early studies examined CF human bronchial epithelial cell responses to *A. fumigatus*. I have also collaborated with other labs on tolerance mechanisms in CF-associated ABPA. More recently, my lab is examining lung disease severity in CF patients that are positive for *A. fumigatus* colonization but do not fit the criteria for ABPA and determining what lung biomarkers correlate with this. In 2011, my laboratory became interested in fungal asthma and specifically identified an immunopathogenic role for the Dectin-1/IL-17A/IL-22 axis in experimental fungal asthma. Since 2012, we have collaborated with the NHLBI Severe Asthma Research Program on inflammatory biomarkers that correlate severity of fungal asthma in humans.

a. Kreindler, J.L.*, [redacted]*, N. Nguyen, Y.R. Chan, J.M. Pilewski, J.F. Alcorn, S.J. Aujla, P. Finelli, M. Blanchard, S.F. Zeigler, A. Logar, E. Hartigan, M. Kurs-Lasky, H. Rockette, A. Ray and [redacted]. Vitamin D3 attenuates Th2 responses to *Aspergillus fumigatus* mounted by CD4+ T cells from cystic fibrosis patients with allergic bronchopulmonary aspergillosis. *Journal of Clinical Investigation* 120:3242-54 (2010). PMID:20714107 *Co-First Author

b. Lilly, L.M., M.A. Gessner, C.W. Dunaway, A.E. Metz, L.M. Schwiebert, C.T. Weaver, G.D. Brown and [redacted]. The beta-glucan receptor Dectin-1 promotes immunopathology during fungal allergy via IL-22. *Journal of Immunology* 189:3653-60 (2012). PMID:22933634

c. Acidic mammalian chitinase has paradoxical contributions to immune responses during acute and chronic fungal exposure. Garth, J.M., J.J. Mackel, K.M. Reeder, J.P. Blackburn, C. W. Dunaway, Z. Yu, S. Matalon, L.J. Fitz and [redacted]. *Infection and Immunity* 2018 Jun 21;86(7). pii: e00944-17.

d. Reeder K.R., C.W. Dunaway, J.P. Blackburn; A.T. Hastie, E.J. Ampleford, D.A. Meyers, and [redacted]. The common γ-chain IL-7 promotes immunopathogenesis during fungal asthma. *Mucosal Immunology* 2018 Jun 15. doi: 10.1038/s41385-018-0028-1.

4. <u>Basic and clinical research: Luminex®-associated collaborations</u>

Having trained as an immunologist, I have long been a proponent of examining and characterizing biomarkers of inflammation, namely cytokines and chemokines. For 15 years, we have employed the Luminex® multiplex protein array-based Bio-Plex® platform from Bio-Rad to quantify cytokines, chemokines and growth factors at the protein level in any type of biospecimen in as little as 25 µl. My lab has become experts in the technology. Between my own research and offering this technology to collaborators, I have published > 65 manuscripts in which Luminex® was employed, more than 20 of which examined inflammatory biomarkers in human samples such as sputum, serum, bronchalveolar lavage fluid and nasal lavage fluid from human diseases such as asthma, COPD, IPF and cystic fibrosis. Examples of these collaborations are listed below.

a. Morris A., T. Alexander, S. Radhi, L. Lucht, F. C. Sciurba, [redacted] and K. A. Norris. Airway obstruction is increased in *Pneumocystis*-colonized HIV-infected outpatients. *Journal of Clinical Microbiology* 47:3773-6 (2009) PMCID: PMC2772636

b. Dostert, C., V. Pétrilli, R. Van Bruggen, [redacted], B.T. Mossman and J. Tschopp. Asbestos and silica activate the Nalp3 inflammasome and trigger innate immunity. *Science* 320:674-677 (2008). PMCID: PMC2396588

c. Gilani, S.R., L.J. Vuga, K.O. Lindell, K.F. Gibson, J. Xue, N. Kaminski, V.G. Valentine, E.K. Lindsey, M. P. George, [redacted] and S.R. Duncan. CD28 downregulation on circulating CD4 T cells is associated with poor prognosis of patients with idiopathic pulmonary fibrosis. *PLoS ONE* 5:e8959 (2010). PMCID: PMC2813297

d. Hastie, A.T., [redacted], C.W. Dunaway, W.C. Moore, B.M. Rector, E.J. Ampleford, H. Li, L. Denlinger, N.N. Jarjour, D.A. Meyers and E.R. Bleecker. Complex association patterns for inflammatory mediators in induced sputum from subjects with asthma. ***Clinical and Experimental Allergy*** (ePub March 9, 2018)

Complete List of Published Work in MyBibliography (110 publications as of January 2018):

http://www.ncbi.nlm.nih.gov/sites/myncbi/[redacted]/bibliography/[redacted]public/?sort=date&direction=ascending

***h*-index**

Scopus: **41** (as of January 1, 2019) https://www.scopus.com/authid/detail.uri?authorId=[redacted]

Google Scholar: **48** (as of January 1, 2019)
http://scholar.google.com/citations?view_op=list_works&hl=en&user=BQcZTsoAAAAJ&gmla=AJsN-F5J8dSICueLrxw3Y-AaDXgYjFtQwF2LXsy5ZQDSQTdahLLprh33OCTW7fxHQk4gpgkW1NvBAPXuzT569O7kwXLDIw3JwiaJeB6RfzZLeHv[redacted]

D. Additional Information: Research Support and/or Scholastic Performance

Active:

R01 HL122426 [redacted] (PI) — 12/01/14 – 11/30/18 (N.C.E. 2019)
National Institutes of Health — $319,764/annual direct dollars
"Immunopathogenesis during fungal asthma"

R01 HL136211 [redacted] (PI) — 01/02/17 – 12/31/20
"Biology of innate IL-22 during lung fungal infection" — $250,000/annual direct dollars

[redacted] [redacted] (PI) — 11/01/16 – 10/31/18 (N.C.E. 2019)
Cystic Fibrosis Foundation — $50,000/annual direct dollars
"The CXCL10/CXCR3 Axis in CF-Related Fungal Exposure"

NIH/NHLBI [redacted] (PI) — 07/01/17 – 06/30/22
"UAB Predoctoral Training Program in Lung Diseases" — $129,327/annual direct dollars
*Note – this grant remains at UAB

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted] Tertiary Mentor: Last name, First name

eRA COMMONS USER NAME: [redacted]

POSITION TITLE: Professor and Chief, Section of Pulmonary, Critical Care and Environmental Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	B.S.	06/1981	Biochemistry
University of Minnesota, Minneapolis, MN	M.D.	06/1985	Medicine
Mayo Grad. School of Med., Rochester, MN		06/1988	Medicine Residency
Duke University, Durham, NC		06/1992	Pulmonary Fellowship

A. Personal Statement.

Understanding the pathogenesis of lung fibrosis has been the focus of my research career, which started at the NIEHS investigating the pathobiology of asbestosis 25 years ago. My recent efforts have been directed toward understanding the role of RNA splicing in promoting fibrogenesis, the effects of latent viral infections and aging on the course of lung fibrosis. My research has also led me into the field of cancer biology. Moreover, in recent years I have published work related to the role of HDACs in fibrogenesis. My efforts have bridged from mechanistic studies in cell culture, to investigations involving animal models, and onward to the design and implementation of investigator-initiated trials in humans. In regard to the current proposal, I have extensive experience in mentoring junior faculty, including prior supervision of a T32 in lung biology. As section chief I have been committed to protecting research time for the development of future physician scientists. I have extensive experience in the conduct of clinical trails pertaining to pulmonary fibrosis. I have enrolled patients into 20 multicenter trials for the treatment of pulmonary fibrosis, and my prior roles in clinical pulmonary fibrosis trials have included PI of a multicenter national trial, steering committee member, data safety monitoring board Chair, adjudication committee member, and site primary investigator. Thus, I have fostered a robust research environment within the Tulane Pulmonary Section, that has the experience and capacity to meet the highest standards of pulmonary research, and I am a well-qualified mentor for Dr. [redacted]'s LA CaTS Roadmap Scholar Program.

B. Positions and Honors

Professional Experience:

2005 – 2014	NIH IPFnet PI for the Gulf South Consortium/Tulane University Medical Center
2004 – date	Professor and Chief, Section of Pulmonary, Critical Care and Environmental Medicine, Tulane University Health Sciences Center, New Orleans, LA.
2005 -2009	Co-PI Multi-center Investigator-Initiated Trial using Imatinib Mesylate for Treatment of IPF
2005-2007	Pulmonary/Critical Care Fellowship Director, Tulane University Medical Center.
2001- 2007	Chief of Pulmonary Medicine at the New Orleans Veterans Administration Hospital.
1999 - 2004	Associate Professor of Medicine with Tenure, Tulane University School of Medicine, New Orleans, LA.
1999 - 2004	Associate Professor of Medicine with Tenure, Tulane University School of Medicine, New Orleans, LA.
1992 - 1993	Associate in Medicine, Duke University Medical Center, Durham, NC.

C. Contribution to Science

Earlier in my career I focused on the cell and molecular biology of pulmonary fibrosis. Initial studies involved the role of platelet-derived growth factor (PDGF) using a murine model of asbestosis. These studies and those of others supported a role for PDGF as a major mitogen for fibroblasts and a key factor in pulmonary fibrosis. Notably, one recently FDA-approved drug for the treatment of IPF blocks PDGF signal transduction. In addition, we were first to implicate connective tissue growth factor (CTGF) in lung fibrogenesis, and there are currently trials exploring the efficacy of an anti-CTGF antibody for the treatment of IPF. My role in manuscript "d" was as Chair of the international data safety monitor board for the trials testing the efficacy of nintedanib for the treatment of IPF. Nintedanib is a treble tyrosine kinase inhibitor and blocks PDGF signal transduction.

a. [redacted], PG Coin, PM Lindroos, LE Ostrowski, AR Brody and JC Bonner. Chrysotile asbestos stimulates increased production of PDGF A-chain by rat lung fibroblasts in vitro. Am. J. Respir. Cell Mol. Biol.,12:162-170, 1995.
b. [redacted], J-Y Liu, B Tonthat, M Friedman, and AR Brody. Upregulation of the PDGF-alpha-receptor precedes the development of asbestos-induced lung fibrosis in rats. Am. J. Respir. Crit. Care Med., 157:1652-1657, 1998.
c. [redacted], L Ortiz, B Tonthat, GW Hoyle, M Corti, G Athas, G Lungarella, AR Brody, and M Friedman. Connective tissue growth factor (CTGF) expression is upregulated in bleomycin-induced lung fibrosis. Am. J. Physiol.; 275:L365-L371, 1998.
d. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, Cottin V, Flaherty KR, Hansell DM, Inoue Y, Kim DS, Kolb M, Nicholson AG, Noble PW, Selman M, Taniguchi H, Brun M, Le Maulf F, Girard M, Stowasser S, Schlenker-Herceg R, Disse B, Collard HR; **INPULSIS Trial Investigators.** Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med. 2014 May 29;370(22):2071-82.
e. Cecilia G. Sanchez, Steven V. Molinski, Rafael Gongora, Meredith Sosulski, Taylor Fuselier, Stephen S. MacKinnon, Richard Wells, Debasis Mondal and [redacted]. The antiretroviral nelfinavir mesylate, a potential therapy for systemic scleroderma. Arthritis Rheumatol. 2017 Sep 21.

I have also been working on implementing clinical trials for IPF in several capacities, including an investigator-initiated trial and those conducted by the NHLBI IPF-net (steering committee member). What is more, I contributed to the work to develop ATS/ERS guidelines for the IPF, and have served as the site PI for over 20 multi-center trials for the treatment of IPF.

a. Craig E. Daniels **&** [redacted], Andrew H. Limper, Kathleen Mieras, Edith Gabor, Darryl Schroeder, Imatinib Treatment for IPF: Randomized Placebo Controlled Trial Results . Am J Respir Crit Care Med. 2010 Mar 15;181(6):604-610.
b. Ganesh Raghu, MD, Kevin J. Anstrom, PhD, Talmadge E. King, Jr., MD, [redacted] Fernando J. Martinez, MD, MS, on behalf of the IPFnet**.** A Double blind, Placebo-Controlled, Randomized Trial of Combined Prednisone, Azathioprine and N-acetyl cysteine in Idiopathic Pulmonary Fibrosis. N Engl J Med. 2012 May 24;366(21):1968-77.
c. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, Colby TV, Cordier JF, Flaherty KR, [redacted] Lynch DA, Ryu JH, Swigris JJ, Wells AU, Ancochea J, Bouros D, Carvalho C, Costabel U, Ebina M, Hansell DM, Johkoh T, Kim DS, King TE Jr, Kondoh Y, Myers J, Müller NL, Nicholson AG, Richeldi L, Selman M, Dudden RF, Griss BS, Protzko SL, Schünemann HJ; on behalf of the ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management.
d. Esposito DB, Lanes S, Donneyong M, Holick CN, [redacted], Lederer D, Nathan SD, O'Quinn S, Parker J, Tran TN.Am J Respir Crit Care Med. 2011 Mar 15;183(6):788-824.Idiopathic Pulmonary Fibrosis in US Automated Claims: Incidence, Prevalence and Algorithm Validation. Am J Respir Crit Care Med. 2015 Aug 4.

More recently my laboratory efforts are concentrated on three areas, namely cytoplasmic effects of HDACs on pathways implicated in fibrogenesis, investigation into the role and diagnostic utility of RNA splicing in fibrogenesis, and mechanisms through which herpes viruses may contribute to malignancy. My clinical experience led us to develop a combination therapy that we believe may be curative for patients afflicted with tumors involving Epstein-Barr virus.

a. Weichao Guo[1], Shigeki Saito[1], Cecilia G. Sanchez[1], Yan Zhuang[1], Rafael E. Gongora Rosero[1], Bin Shan[2], Fayong Luo[3], [redacted]. TGF-β1 Stimulates HDAC4 Nucleus to Cytoplasm Translocation and NADPH Oxidase4-Derived Reactive Oxygen Species in Normal Human Lung Fibroblasts. Am J Physiol Lung Cell Mol Physiol. 2017 Jun 1;312(6):L936-L944.
b. Mark D Sides, Meredith L Sosulski, Fayong Luo, Zhen Lin, Erik K Flemington and [redacted]. Co-treatment with Arsenic Trioxide and Ganciclovir Reduces Tumor Volume in a Murine Xenograft Model of Nasopharyngeal Carcinoma. BMC Cancer. Virol J. 2013 May 16.
c. Qinyan Yin, Mark Sides, Christopher Parsons, Erik Flemington and [redacted]. Arsenic Trioxide inhibits EBV reactivation and promotes cell death in EBV-positive lymphoma cells. Submitted, Virol J. 2017 Jun 21;14(1):121.
d. Shigeki Saito, Yan Zhuang, Bin Shan, Svitlana Danchuk, Fayong Luo, Martina Korfei, Andreas Guenther, and [redacted]. Tubastatin, a "selective" HDAC6 deacetylase inhibitor, represses type-1 collagen expression in TGF-β1-treated lung fibroblasts and bleomycin-treated mouse lungs. PLoS One. 2017 Oct 18;12(10).
e. Shigeki Saito, Yan Zhuang, Takayoshi Suzuki, Yosuke Ota, Marjorie E. Bateman, Ala L. Alkhatib, Gilbert F. Morris, and [redacted]. HDAC8 inhibition ameliorates pulmonary fibrosis, J Physiol Lung Cell Mol Physiol. 2018 Oct 25.

Public Bibliography (98 PubMed citations)
https://www.ncbi.nlm.nih.gov/sites/myncbi/1hut_59_dw-ofb/bibliography[redacted]/public/?sort=date&direction=ascending

D. Research Support

Current Support
Aging COBRE Pilot Grant (July 1, 2018 – June 30, 2019) 2 calendar months
Role on Pilot Project PI.
COBRE PI S. Michal Jazwinski
$50,000

Completed Research Support

2012-2018 PI
The Wetmore Foundation
Mechanisms involved in the propensity for fibrogenesis in the aging lung

2012-2014 Co-Investigator
NIH U01HL105371
Phase II Study of Inhaled Carbon Monoxide for the Treatment of IPF

2010-2012 Co-Investigator
National Institutes of Health R21 Research Grant
Role of Heperan Sulfate 6-O-Endosulfatae 1 and 2 in Pulmonary Fibrosis

2006-2010 Principal Investigator
National Institutes of Health R01 Research Grant
Role of EBV Gene Products in Lung Fibrogenesis

2005-2010 Principal Investigator
National Institutes of Health R01 Research Grant
Viral Protein Mediator of HIV-Related Pulmonary Hypertension

2005 – 2013 Site Director
National Institutes of Health IPF Clinical Research Network

2003 – 2015 PI/Director
National Institutes of Health T32 Pulmonary Disease Training Grant, 2003-2014
Training in Lung Molecular and Cell Pathobiology

ABSTRACT:

Cystic fibrosis (CF) affects over 30,000 people in the United States and more than 70,000 people worldwide. A predominant feature of the clinical syndrome of CF and non-CF bronchiectasis is chronic infections of the lung and sinus with key pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Chronic infections with these pathogens are a major cause of morbidity and mortality in patients with CF, leading to decreased lung function and lowered survival rates. Importantly, chronic sinus disease in CF is a known risk factor not only for disease progression, but also for complications such as graft colonization and rejection following transplantation. Despite significant prevalence and disease burden, the mechanisms underlying bacterial persistence remain poorly understood. The cytokine interleukin-22 (IL-22) is produced by several subsets of immune cells and plays an important role in mucosal immunity against microbes at the epithelial barrier by binding to its heterodimeric receptor complex and regulating the production of host anti-microbial proteins. We propose here to study a potential new therapeutic target: interleukin-22 binding protein (IL-22 BP). IL-22 BP is a soluble decoy receptor encoded by the *Il22Ra2* gene with strong affinity to IL-22, thereby acting as a natural IL-22 antagonist. It has been shown that IL-22 BP is expressed in the lung and upper airway including the nose. Little is otherwise known about this protein's functional role in the airways. Preliminary data from our lab has shown that IL-22 BP levels are markedly increased in lung samples (bronchoalveolar lavage, lung tissue, and lymph nodes) as well as in sinus washes from patients with CF. This was not observed in patients with allergic sinusitis. Furthermore, high protein levels of IL-22 BP were associated with the presence of *S. aureus* or *P. aeruginosa* positive cultures obtained from CF patients. The goal of this proposed research is to test the hypothesis that IL-22 BP is in fact causal in mediating bacterial persistence in the airway. Using a novel humanized IL-22 BP transgenic murine model that overexpresses IL-22 BP as well as human samples, we will move beyond associating and determine whether the IL-22 pathway and the presence of increased IL-22 BP affects chronic infection and colonization. Through the use of advanced techniques such as qPCR, ELISA, and RNAseq analyses, we will further characterize this protein and the expression pathways implicated in host response to infection with *S. aureus*. We will test the hypothesis that increased levels of IL-22 BP decreases host responses mediated by IL-22 thereby promoting chronic infection. This has important clinical implications as this proposal explores the potential role of a unique pathway that may identify a novel therapeutic target in the treatment of patients with CF.

PROPOSED PERFORMANCE SITE:

Tulane University School of Medicine
Center for Translational Research in Infection and Inflammation

Patient Recruitment:
Tulane University Medical Center

NAMES and ROLES of MENTORS:

- [redacted], **MD:** Professor of Medicine and Pediatrics and Director of the Tulane University School of Medicine's Center for Translational Research in Infection and Inflammation. Dr. [redacted] will serve as Dr. [redacted]'s primary mentor providing guidance on basic and translational research focusing on the role of IL-22 BP in chronic lung infection. He will chair her Advisory Committee and also meet with her on a weekly basis for direct one-on-one discussions and training.

- [redacted], **PhD:** Professor and Chair of the Department of Microbiology and Immunology. Dr. [redacted] will serve on the Advisory Committee for Dr. [redacted].

- [redacted], **MD:** Professor and Chief of the Section of Pulmonary Diseases, Critical Care and Environmental Medicine. Dr. [redacted] will provide professional development guidance and serve on the Advisory Committee for Dr. [redacted].

RESEARCH PROPOSAL

SPECIFIC AIMS

Cystic fibrosis (CF) results from mutations within the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene and is a leading inherited cause of morbidity and mortality in the Caucasian population. In the United States, approximately 30,000 individuals are affected by this progressive and fatal disease[1]. Pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most common pathogens isolated from patients with CF[1]. Abnormal immune responses to pathogen exposure in patients with CF are being more widely recognized as a major contributor to disease morbidity and mortality[2,3]. For example, it has been shown that patients with CF generate robust populations of pathogen specific, yet ineffective, IL-22 producing T-cells within the lung and lymph node[4].

IL-22 binding protein (IL-22 BP, also known as IL-22RA2) is a soluble decoy receptor with strong affinity to IL-22 acting as a natural IL-22 antagonist and potent neutralizer. Preliminary data from our lab has shown that IL-22 BP protein levels are substantially increased in lung samples (bronchoalveolar lavage fluid, lung tissue, and lymph nodes) as well as in sinus washes from patients with CF-related sinus disease. Furthermore, high IL-22 BP levels were observed in CF-related sinusitis due to *S. aureus* or *P. aeruginosa* infection. Here, we aim to further explore the factors that favor persistent infection with *S. aureus* in patients with CF. Using both a mouse model and human samples, we will determine whether the IL-22 pathway and the presence of increased IL-22 BP affects infection and colonization. **We hypothesize that increased levels of IL-22 BP decreases the host response mediated by IL-22 at the mucosal barrier thereby promoting chronic infection.** This has important clinical implications and may identify a novel therapeutic target. The proposed study capitalizes on the excellent research infrastructure of the Tulane Center for Translational Research in Infection and Inflammation, direct access to a unique patient population, and the established track record of the applicant's mentorship team in promoting the development of young translational scientists. The following Specific Aims, based on studies in both transgenic mice and human samples, will critically test our hypothesis using a translational approach:

Aim 1: Establish whether IL-22 BP is independently associated with higher rates of infection with *S. aureus* in a novel humanized transgenic mouse model.
Approach: In order to test the hypothesis that increased levels of IL-22 BP will promote increased rates of sinopulmonary infection, we have generated a novel humanized transgenic mouse model that overexpresses human IL-22 BP that binds to both murine and human IL-22. We will inoculate these mice (or transgene negative littermate controls) with *S. aureus* intranasally and compare the rates of sinopulmonary infection and bacterial clearance. As a positive control we will use IL-22$^{-/-}$ mice.

Aim 2: Establish the pathways for alteration in disease response in the setting of increased IL-22BP.
Approach: We will use advanced techniques such as qPCR, ELISA, and RNA-Seq analyses of total lung and lymphoid tissue including nasal associated lymphoid tissue (NALT) to study the markers and differential expression pathways implicated in host response to infection with *S. aureus* in mice with overexpressed IL-22 BP as compared to IL-22 $^{-/-}$ and transgene negative littermate controls.

Aim 3: Establish if, where, and to what degree IL-22 BP is expressed in human patients with CF in an independent cohort.
Approach: Our prior data is from the CF Center in Pittsburgh, PA. To extend this data to the Tulane University CF center, IL-22 BP levels in serum, sputum, and sinus samples will be measured during the course of the study period in addition to performing CF routine bacterial cultures. This data will be compared to human control subjects without a diagnosis of cystic fibrosis, but with chronic rhino-sinusitis.

Significance and Innovation

A predominant feature of the clinical syndrome of CF and non-CF bronchiectasis is chronic infections and colonization with key pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* leading to increased rates of pulmonary exacerbations, decreased lung function and lower survival rates. Chronic sinus disease in CF is a known risk factor for disease progression and the upper airways are a recognized reservoir for graft colonization and rejection after lung transplant [5]. Despite the great strides that have been made in gene modulation therapy in CF, there remains a large gap in our understanding of the immunological and microbiological factors that predispose these patients to chronic lung infection [6,7].

Initial failure to eradicate bacteria in the lungs with CF has been linked to reduced HCO3- transport through CFTR [8-10]. However, this does not fully explain bacterial persistence within the airway. Chan and colleagues have shown that patients with CF generate robust T-cell and B-cell responses to specific pathogens, but that these responses are insufficient to eradicate infection [4]. This may in part be due to cytokine mediated defective ion transport within the epithelium such as IL-17A as part of the adaptive immune response [9]. The cytokine interleukin-22 (IL-22), a member of the IL-10 superfamily, is produced by several subsets of immune cells including T helper (Th17, Th22 cells) and innate lymphoid cells (ILCs). IL-22 plays a key role in innate host defense against microbes at the epithelial barrier by binding to its heterodimeric receptor complex composed of IL-22R1 and IL-10R2 (IL-10 R beta). This cytokine has been shown to play an important role in infection with such pathogens as *Klebsiella pneumoniae*, *Aspergillus fumigatus*, *Streptococcus pneumoniae*, and influenza[11-18]. IL-22 also plays a critical role in bacterial clearance in a nasal colonization model with *S. aureus* [19]. IL-22 binding protein (IL-22 BP, also known as IL-22RA2) is a soluble decoy receptor with strong affinity to IL-22 (20- to 1000- fold higher affinity as compared to its binding to IL-22R1) acting as a natural IL-22 antagonist and potent neutralizer. It has been shown that IL-22 BP is expressed in the epithelial cells of both the alveoli and the upper airways and is basally expressed within the nasal mucosa [20]. Still, little is known about the functional role of IL-22 BP in the lung and upper airway. Furthermore, it is unclear whether effects associated with IL-22 BP are due solely to IL-22 neutralization or whether other mechanisms are involved.

These studies are highly ***innovative*** because they are the first to investigate the role of IL-22 BP in chronic sinopulmonary infection in a significant and particularly disease burdened patient population. In order to study this protein further, our lab recently generated a ***novel*** humanized transgenic mouse model that overexpresses IL-22 BP. Lastly, our proposal explores the potential role of ***different*** *and* ***unique*** pathways in the establishment of chronic infection with pathogens such as *S. aureus* that may provide new and important targets for future therapeutic trials.

Research Approach

Murine studies (Aims 1 and 2)

Rationale: To determine if increased levels of IL-22 BP cause greater susceptibility to *S. aureus* infection or perturbs clearance, our lab recently generated a novel humanized IL-22 BP transgenic mouse model that overexpresses IL-22 BP to a similar level to that observed in CF patients (~ 60 ng/ml). Using these transgenic mice, we aim to further elucidate the role of IL-22 BP in host defense and in chronic infection in this patient population.

Experimental Approach: 6-8-week-old transgenic mice with overexpression of IL-22 BP, as well as positive control IL-22 $^{-/-}$ mice and transgene negative littermate controls, will be inoculated with streptomycin resistant *S. aureus* strain Newman intranasally. We will plan on euthanasia and tissue harvest at 4 different time points post-inoculation (day 1, day 3, day 7, and day 14). Nasal/sinus and lung tissues will be homogenized and plated for culture to determine relative bacterial burden. Cytokine expression will be determined through ELISA or qPCR techniques measuring mRNA levels. Flow cytometry will be used to determine if IL-22BP overexpression affects recruitment of neutrophils or inflammatory monocytes that are critical for bacterial clearance. Additionally, we will assess the expression of antimicrobial genes regulated by IL-22, including S100A8, S100A9, and regenerating

islet derived gamma. RNAseq techniques will be applied to the different tissue sites as well to provide an unbiased assessment of mucosal immunity.

Human patient population: (Aim 3)

Rationale: Preliminary data has shown significantly higher levels of IL-22 BP in the lung and sinus washings of patients with CF.

Experimental Approach: In order to confirm this prior observation, sputum, serum, sinus samples will be obtained from patients with cystic fibrosis and measurements of IL-22 BP will be measured. Bacterial cultures will also be collected in parallel to monitor rates of infection and/or colonization. We will also recruit patients diagnosed with chronic rhinosinusitis in the absence of cystic fibrosis to serve as controls. With the samples that we are able to obtain, we will also perform transcriptome studies in order to gain a deeper understanding of IL-22 BP production and function in humans. We will also examine whether IL-22 BP can be saturated with recombinant IL-22 and assay its bioactivity in an IL-22 reporter cell line as previously described [21].

Utilization of LA CaTS resources: Consultation with the LA CaTS Biostatistics and Epidemiology Core has been initiated in order to determine optimum numbers needed for this study. We will also plan to utilize the Tulane Clinical Translational Unit to help with sample collection from the human patient population including blood draws. The LA CaTS Center REDCap software will be used for data capture and analysis.

Anticipated Results: We anticipate that IL-22 BP overexpression will lead to increased susceptibility to infection with *S. aureus*. Though little is known about IL-22 BP, we predict that this effect will be due to decreased functional IL-22 thereby impacting the IL-22 pathway. We further predict that IL-22 supplementation in these mice will lessen these negative effects and/or decrease rates or severity of infection. In addition, we expect to prove that increased levels of IL-22 BP are present in human patients with cystic fibrosis thereby identifying a potential therapeutic target.

These studies will provide essential preliminary and feasibility data for a NIH K mentored award. Importantly, this work will also provide me with a new knowledge base and skillset distinct from those acquired previously as this work requires learning new bench techniques. Importantly, this work will also further my understanding of translational study design.

Potential Pitfalls and Alternative Approaches: In a recent study by Bayes et al, the absence of IL-22 in knock-out mice resulted in no significant differences in acute mortality, bacterial burden, chronic infection rates, histological changes or neutrophil inflammation in a model of chronic *P aeruginosa* infection [22]. This would go against our hypothesis that IL-22 BP exerts its effects solely through alteration of the IL-22 pathway. As very little is understood about IL-22 BP, our studies to identify the mechanistic and functional pathways associated with IL-22 BP will still be an important contribution to science by furthering our understanding of this protein.

Human patient recruitment may be difficult especially in recruiting a matched control group as we do not have regular or direct access to this patient population. In order to address this, we will likely need to work closely with the patient populations in Tulane's Otolaryngology and Allergy/Immunology departments to ensure adequate enrollment. Utilizing the LA CaTS resources such as the CTU will additionally help in this regard. Furthermore, working with these other disciplines further promotes the mission of the LA CaTS by fostering multi-disciplinary collaboration in translational research efforts.

CAREER DEVELOPMENT PLAN:

Participation in the Louisiana Clinical and Translational Science (LA CaTS) Roadmap Scholars program is a critical aspect of my development as a junior faculty member and physician-scientist of Tulane University within the Section of Pulmonary Diseases, Critical Care and Environmental Medicine. From my start as a research fellow at the NIH, studying genetic variations in immunologic factors predisposing to the development of macular degeneration, to the dedicated research time focusing on neutrophil biology and innate host response to E-cigarette vapor exposure during my pulmonary and critical care fellowship as an appointee on the UCSD T32 training grant, my application to this program represents a decisive point in my progression towards becoming an independent clinician-scientist focused on lung immunology. It is at Tulane University that I am finally able to combine my research interests in immunology and inflammation with my area of clinical focus and expertise, cystic fibrosis and non-cystic fibrosis bronchiectasis. I believe that pursuing this award is not only a natural progression of my background and career development, but a critical step in achieving my long term goal of becoming an independent clinician-investigator.

With the framework and support provided by the LA CaTs program, and with the guidance of my identified mentorship team, I am now focusing on the role of IL-22 BP in host responses and the development of chronic infections with *S. aureus*. This is translational research involving transgenic mouse models and human samples that may result in important therapeutic interventions for the patients that I care for on a daily basis. This program will allow me to dedicate the necessary time and effort needed to develop and grow in this new area of research, ensuring the support required to obtain the preliminary data needed to develop a local research program and obtain external funding. In addition to preliminary project completion, this protected time will allow for advanced coursework through the Master of Science in Clinical Research (MSCR) program, an area that I identify as a need in my background. This will total 38 credit hours and will include courses such as Introduction to Biostatistics (BIOS 6030), Epidemiologic Methods (EPID 6030), Protocol Design and Writing (MSCR 6440), and Grant Writing (MSCR 7090). Participation in the LA CaTS program will further provide a rich and stimulating network for scientific collaboration with like-minded individuals and peers. This will not only strengthen my understanding of success in academic medicine, but will serve the mission of LA CaTS by promoting the future of translational research in Louisiana.

During the course of this award (Table 1), and in addition to the framework provided by the LA CaTS program, I will meet with my primary mentor weekly as well as attend weekly labs meetings. I will also meet with my mentorship committee quarterly to discuss overall progress and address obstacles or challenges. I will present bi-annually at Tulane's Lung Biology research meeting and will submit my work to national and international meetings in order to disseminate ideas and to collaborate in this area of focus. I will become more involved with The American Society for Clinical Investigation (ASCI) and attend the annual meeting. Additionally, I will also apply for the AAMC Early Career Women Faculty Leadership Development Seminar in 2019.

In short, I believe that my prior research training and publication record, my strong and outstanding multidisciplinary mentorship team, and the research and scientific infrastructure at Tulane make me an ideal candidate for the LA CaTS Roadmap Scholars Program. I am certain that my participation in this program will ensure an exceptional foundation for an NIH K mentored Career Development Award or equivalent and will be invaluable as I work toward my goal of becoming an independent investigator studying innate host responses to chronic diseases.

Table 1: Award Project Timeline	July 2019-June 2021 (Quarters)							
	1	2	3	4	5	6	7	8
AIMS 1&2								
Data Collection and Analysis	X	X	X	X				
Dissemination*		X	X	X	X			
AIM 3								
Data Collection and Analysis	X	X	X	X				
Dissemination*			X	X	X			
Grant Preparation:								
K08 preparation and Submission					X	X	X	X
MSCR Coursework (Totaling 38 credit hours for completion)	X	X	X	X	X	X	X	X
* Manuscript preparation/submission, presentation at national meetings								

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Tulane University

SCHOOL OF MEDICINE

Department of Medicine
Section of Pulmonary Diseases, Critical Care
And Environmental Medicine

January 28th, 2019

Vivian Fonseca, MD
Paula Gregory, PhD
Phillip Brantley, PhD
Directors, LA CaTS Professional Development Core

Re: [redacted] MD, Roadmap Scholars Program Applicant

Dear Drs. Fonseca, Gregory, and Brantley,

As the Section Chief of Pulmonary Diseases, Critical Care, and Environmental Medicine at Tulane University School of Medicine, I am pleased to write this letter of support for Dr. [redacted] and her application to the LA CaTS Roadmap Scholar Program.

Dr. [redacted] is a motivated and focused junior investigator who recently joined our section with the clear aim of developing as a clinician-scientist. Her long-standing dedication to academic medicine and to advancing the sciences is clearly supported by her CV. As a member of her direct mentorship committee, I have reviewed her proposal entitled "The Role of IL-22 Binding Protein in Sinopulmonary Infection and Colonization with Staphylococcus Aureus" and believe that she is the ideal candidate for further translational research training as a LA CaTS Roadmap Scholar.

I pledge the support of the Section of Pulmonary Disease, Critical Care, and Environmental Medicine in the career development of Dr. [redacted] as a Roadmap Scholar. I intend to extend financial support towards a laboratory technician and for research supplies. Dr. [redacted] will have 75 percent protected time for the first two years of this award and for up to an additional three years with the expectation that she will transition to a K award. In the event that she is selected as a Roadmap Scholar her VA eighths will be decreased in order to afford her 75% protected time. Dr. [redacted] has my full and enthusiastic support in her application to become a LA CaTS Roadmap Scholar.

Sincerely,

[redacted]
Deming Internal Medicine Endowed Chair, Professor of Medicine
Section Chief of Pulmonary Disease, Critical Care and Environmental Medicine
Tulane University School of Medicine

Tulane University

SCHOOL OF MEDICINE

Department of Medicine
Section of Pulmonary Diseases, Critical Care and Environmental Medicine

January 24th, 2019

Vivian Fonseca, MD
Paula Gregory, PhD
Phillip Brantley, PhD
Directors, LA CaTS Professional Development Core

Re: [redacted] MD
Roadmap Scholars Program Applicant

Dear Drs. Fonseca, Gregory, and Brantley,

As Chair of the Department of Medicine at Tulane University School of Medicine, I am pleased to write this letter of support for Dr. [redacted] and her application to become a LA CaTS Roadmap Scholar.

Dr. [redacted] is a bright and motivated junior investigator who recently joined our department as Assistant Professor. I believe she has a promising future in translational research as a clinician-scientist as evidenced by her CV. I have reviewed her proposal entitled "The Role of IL-22 Binding Protein in Sinopulmonary Infection and Colonization with Staphylococcus Aureus" and feel that she is an outstanding candidate for further research training as a LA CaTS Road Map Scholar.

I pledge the support of the Department of Medicine in the career development of Dr. [redacted] as a Roadmap Scholar. Through the Section of Pulmonary Diseases, Critical Care, and Environmental Medicine, Dr. [redacted] will have 75 percent protected time for the first two years of this award and for up to an additional three years if she gains support for further training with a K award.

Dr. [redacted] has my enthusiastic support in her application to become a LA CaTS Roadmap Scholar.

Sincerely,

[redacted]

The Harry B. Greenberg Chair of Medicine
Professor of Medicine
Tulane University School of Medicine

Tulane University

January 29, 2019

SCHOOL OF MEDICINE

L. Lee Hamm, MD
Senior Vice President & Dean, School of Medicine
James R. Doty Distinguished Professor and Chair

Vivian Fonseca, MD
Paula Gregory, PhD
Phillip Brantley, PhD
Directors, LA CaTS Professional Development Core

RE: [redacted], MD Roadmap Scholars Program Applicant

Dear Drs. Fonseca, Gregory, and Brantley,

As Dean of the Tulane University School of Medicine, it is a pleasure to provide my strong support for Dr. [redacted] in her application to become a LA CaTS Roadmap Scholar.

Dr. [redacted] is a recently appointed Assistant Professor within the Section of Pulmonary Diseases, Critical Care, and Environmental Medicine at Tulane University School of Medicine. She joined Tulane University with the clear motivation to develop as a clinician-scientist. She is an exceptional candidate and her commitment to, and passion for, academic medicine is evidenced by her CV. I have reviewed her proposal entitled "The Role of IL-22 Binding Protein in Sinopulmonary Infection and Colonization with Staphylococcus Aureus" and feel that she is an outstanding candidate for further translational research training as a LA CaTS Roadmap Scholar.

I am excited about Dr. [redacted]s future as an academic faculty member and I pledge the support of the Tulane School of Medicine in her career development as a Roadmap Scholar. Through the Section of Pulmonary Diseases, Critical Care, and Environmental Medicine, Dr. [redacted] will have 75 percent protected time for the first two years of this award and for up to an additional three years if she earns the support for further training with a K award.

Dr. [redacted] has my enthusiastic and unreserved support in her application to become a LA CaTS Roadmap Scholar.

Sincerely,

[redacted]

L. Lee Hamm III, MD, FACP
Senior Vice President & Dean of the School of Medicine
The James R. Doty Distinguished Professor and Chair

LLH/dlg

SCHOOL OF MEDICINE

Department of Medicine
Center for Translational Research in Infection and Inflammation

[redacted], MD
Professor of Medicine and Pediatrics
John W Deming Endowed Chair in Internal Medicine
Director, Center for Translational Research in Infection and Inflammation

January 28th, 2019

Vivian Fonseca, MD
Paula Gregory, PhD
Phillip Brantley, PhD
Directors, LA CaTS Professional Development Core

Re: [redacted] MD
Roadmap Scholars Program Applicant
Mentor Letter of Support

Dear Drs. Fonseca, Gregory, and Brantley,

As her primary mentor, I am happy to write this letter of enthusiastic support for Dr. [redacted] and her application to the LA CaTS Roadmap Scholar Program. I am excited to continue working with Dr. [redacted] in a mentoring capacity and I am committed to supporting her development as a young clinician-scientist. I believe that she will excel as Roadmap Scholar and feel that the support provided by this program will be invaluable to her continued growth as junior faculty here at Tulane University.

I have critically reviewed her proposal entitled “The Role of IL-22 Binding Protein in Sinopulmonary Infection and Colonization with Staphylococcus Aureus” and feel that she is truly an outstanding candidate for further translational research training as a LA CaTS Roadmap Scholar. Through this project, she is able to capitalize and expand on her background in basic bench and translation research in combination with her area of clinical expertise, cystic fibrosis and non-cystic fibrosis bronchiectasis. Furthermore, she has identified an incredibly strong mentorship team - one that will not only be able to provide excellent scientific guidance and critique, but also one that is able to provide the counseling needed for successful career development in academic medicine. I am the ideal mentor for Dr. [redacted] given my extensive background and internationally recognized expertise in lung immunology and inflammation, particularly in my contributions towards the understanding of the cytokine IL-22. I also have a long record of accomplishment of successfully mentoring young trainees. I have trained many post-doctoral fellows as well as junior faculty and have served as the sponsor for 6 K08/K01 awards. I have also mentored several junior faculty members in their successful attainment of independent funding at the R01 level.

I am confident that Dr. [redacted] will excel as Roadmap Scholar and exceed the expectations set forth by this wonderful program. Dr. [redacted] has incredible promise and potential in academic medicine as a young clinician-scientist. At this early stage in her career, she has shown the consistent eagerness and enthusiasm needed to succeed in academia. She has

been recognized previously through the competitive honors of receiving an NIH post-baccalaureate intramural research training award (IRTA) fellowship, her appointment as Chief Fellow and her appointment to her previous institution's NIH T-32 training grant. Her CV, with over 50 publications and abstract presentations, many as first author, reflects her ability to see projects through to completion. Her involvement on both local and national levels in leadership roles, reflects her desire to disseminate and collaborate information and academic progress.

Dr. [redacted] has built a foundation in the sciences through her work in both basic bench and translational research as well as through her participation in multi-center trials as either the principal site investigator or as sub-investigator. She has demonstrated her commitment to advancing the field of medicine and her passion for academia. Participation in the Roadmap Scholar Program will ensure the protection and support needed to ensure that Dr. [redacted]'s continued development towards becoming an independent clinician-scientist within Tulane University. I have no doubt that she will succeed as a LA CaTS Roadmap Scholar and I strongly support and encourage her acceptance into this program without reservation.

Sincerely,

[redacted]

[redacted]

School of Medicine
Chad Steele, Ph.D.
Professor and Chair
Department of Microbiology and Immunology

January 28, 2019

Vivian Fonseca, MD
Paula Gregory, Ph.D.
Phillip Brantley, Ph.D.
Directors, LA CaTS Professional Development Core

RE: [redacted] MD
Roadmap Scholars Program Applicant
Mentor Letter of Support

Dear Drs. Fonseca, Gregory and Brantley,

I am pleased to offer this letter of enthusiastic support for Dr. [redacted] and her application to the LA CaTS Roadmap Scholar Program. As a member of her mentorship committee, I am excited to work more closely with Dr. [redacted] in a mentoring capacity and am committed to supporting her development as a young clinician-scientist.

As a member of her mentorship committee, I have reviewed her proposal entitled "The role of IL-22 binding protein in sinopulmonary infection and colonization with *Staphylococcus aureus*" and feel that she is truly an excellent candidate for further translational research training as a LA CaTS Roadmap Scholar. I am an ideal member of her mentorship committee given my extensive background and expertise in lung immunology and infectious disease with a focus on the cytokine IL-22. Moreover, I also have a long track record of successfully mentoring junior trainees, including 9 Ph.D. students, 7 post-doctoral fellows, 3 clinical fellows and 4 junior faculty members. Along with the support of the other members of her mentorship team, I am confident that Dr. [redacted] will excel as Roadmap Scholar.

I have reviewed her CV and am impressed by her scholarly activity and achievement at such an early stage in her career with over 50 publications and abstract presentations at national and international conferences. She has shown an eagerness to learn and has shown self-motivation in building a strong foundation in the sciences. She has done work in both basic bench and translational research as well as participated in multi-center trials as either the principal site investigator or as sub-investigator. She has demonstrated her commitment to advancing the field of medicine and her ability to be highly productive in a research setting during relatively short periods of time while training at the NIH as a post-baccalaureate intramural research training award (IRTA) fellow and during her final year of training as an appointee on her previous institution's NIH T32 training grant, both of which are considered competitive honors.

Dr. [redacted] is clearly highly motivated and joined Tulane University as a junior faculty member directly out of her sub-specialty training. Participation in the Roadmap Scholar Program will ensure the protection and support that Dr. [redacted] needs in order to continue developing towards becoming an independent clinician-scientist within her new institution. I have no doubt that she will exceed expectations as a LA CaTS Roadmap Scholar and I support and encourage her acceptance into this program without reservation.

Sincerely,

[redacted]

Professor and Chair
Department of Microbiology and Immunology
School of Medicine
Tulane University
1430 Tulane Avenue, Room 5053
New Orleans, LA 70112
Telephone: (504) 988-5386
Fax: (504) 988-5144
Email: [redacted]

Tulane University

SCHOOL OF MEDICINE

Department of Medicine
Section of Pulmonary Diseases, Critical Care
And Environmental Medicine

January 28th, 2019

Vivian Fonseca, MD
Paula Gregory, PhD
Phillip Brantley, PhD
Directors, LA CaTS Professional Development Core

Re: [redacted] MD
Roadmap Scholars Program Applicant
Mentor Letter of Support

Dear Drs. Fonseca, Gregory, and Brantley:

As the Section Chief of Pulmonary Diseases, Critical Care, and Environmental Medicine at Tulane University School of Medicine, and as a member of her mentorship committee, I am writing this letter of enthusiastic support for Dr. [redacted] and her application to the LA CaTS Roadmap Scholar Program.

Dr. [redacted] shows great promise as a young clinician-scientist. I first met Dr. [redacted] during her residency training in New Orleans and was pleased to have her join our faculty here at Tulane University upon completion of her fellowship training. Dr. [redacted] is a motivated and focused junior investigator who recently joined our section with the clear aim of developing as a clinician-scientist. At this early stage in her career, her impressive dedication to academic medicine and toward advancing the sciences is evidenced by her CV with over 50 publications and abstract presentations, many as first author. Her early research while at the NIH as an intramural research training award fellow and at her prior institution as Chief Fellow and appointee to the institutional T-32 training grant, she has worked to build the foundation for a successful career in academic medicine as a researcher. She is an ambitious junior faculty member who is already establishing herself as a leader on a national level through her involvement with the American Thoracic Society. Furthermore, she is also a dedicated clinician caring for patients with cystic fibrosis, a patient population directly tied to her research focus. As a member of her direct mentorship committee, I have reviewed her proposal entitled "The Role of IL-22 Binding Protein in Sinopulmonary Infection and Colonization with Staphylococcus Aureus" and believe that she is the ideal candidate for further translational research training as a LA CaTS Roadmap Scholar. I am eager to assist Dr. [redacted] in a mentoring capacity and I enthusiastically support her potential as a LA CaTS Roadmap Scholar.

As Section Chief, I commit the support of the Section of Pulmonary Disease, Critical Care, and Environmental Medicine toward the career development of Dr. [redacted] as a Roadmap Scholar. As a mentor, I am further

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Department of Medicine
Section of Pulmonary Diseases, Critical Care
And Environmental Medicine

committed to her development as a young clinician-scientist. I am confident that Dr. [redacted] will meet the expectation that she will achieve further training support with a K award or equivalent. She is also eligible for a VA Career Development Award. Dr. [redacted] has my utmost support in her application to become a LA CaTS Roadmap Scholar and my complete confidence as she embarks upon a promising scholarly career in academic medicine as a clinician-scientist.

Sincerely,

[redacted]

Deming Internal Medicine Endowed Chair, Professor of Medicine
Section Chief of Pulmonary Disease, Critical Care and Environmental Medicine
Tulane University School of Medicine

Health Sciences Center
1430 Tulane Ave., SL-9, New Orleans, LA 70112-2699 *tel* 504.988.2250 *fax* 504.988.2144 www.tulane.edu

Mentorship Agreement

[1] ***Goals*** (what you hope to achieve as a result of this relationship; e.g., gain perspective relative to skills necessary for success in academia, explore new career opportunities/alternatives, obtain knowledge of organizational culture, networking, leadership skill development, etc.):

My goal is to acquire the skillset needed to succeed in academic medicine as a clinician-scientist by continuing to build my fund of knowledge, exploring new methods to scientifically approach clinical challenges, and by strengthening my grant writing skills. My immediate goal is to gain support as a Roadmap Scholar.

[2] ***Steps to achieving goals*** as stated above (e.g., meeting regularly, manuscripts/grants, collaborating on research projects, steps to achieving independence, etc.):

In order to achieve the above goals, I will plan on meeting with my mentorship team regularly to review my progress. I will be proactive in submitting abstracts to local and national meetings and in grant and manuscript preparation. I will also strengthen my translation research skillset through MSCR coursework.

[3] ***Meeting frequency*** (frequency, duration, and location of meetings):

I will meet with my entire mentorship committee in person quarterly to review my progress and to address any setbacks for no less than one hour in the JBJ bldg. I will meet with my primary mentor weekly and also attend weekly lab meetings.

[4] ***Confidentiality:*** Any sensitive issues that we discuss will be held in the strictest of confidence. Issues that are off limits for discussion include:

None identified at this time.

[5] Plan for ***evaluating relationship effectiveness*** (e.g., bi-annual review of mentorship meeting minutes, goals, and outcomes/accomplishments):

I will plan to meet with my primary mentor weekly. Quarterly, together we will review and evaluate the effectiveness of our mentor/mentee relationship and establish tangible goals for the following quarter.

[6] ***Relationship termination clause****:* In the event that either party finds the mentoring relationship unproductive and requests that it be terminated, we agree to honor that individual's decision without question or blame.

[7] ***Duration****:* This mentorship relationship will continue as long as both parties feel comfortable with its productivity or until:

I have successfully competed for a non-mentored award.

Mentee's Signatu[redacted] Date 01/20/15

Mentor's Signature [redacted]

Mentorship Agreement

[1] ***Goals*** (what you hope to achieve as a result of this relationship; e.g., gain perspective relative to skills necessary for success in academia, explore new career opportunities/alternatives, obtain knowledge of organizational culture, networking, leadership skill development, etc.):
My goal is to acquire the skillset neeeded to succeed in academic medicine as a clinician-scientist by continuing to build my fund of knowledge, exploring new methods to scientifically approach clinical challenges, and by strengthening my grant writing skills. My immediate goal is to gain support as a Roadmap Scholar.

[2] ***Steps to achieving goals*** as stated above (e.g., meeting regularly, manuscripts/grants, collaborating on research projects, steps to achieving independence, etc.):
In order to achieve the above goals, I will plan on meeting with my mentorship team regularly to review my progress. I will be proactive in submitting abstracts to local and national meetings and in grant and manuscript preparation. I will also strengthen my translation research skillset through MSCR coursework.

[3] ***Meeting frequency*** (frequency, duration, and location of meetings):
I will meet with my entire mentorship committee in person as needed and, more formally, quarterly to review my progress and to address any setbacks for no less than one hour in the JBJ 2nd floor conference room.

[4] ***Confidentiality:*** Any sensitive issues that we discuss will be held in the strictest of confidence. Issues that are off limits for discussion include:
None identified at this time.

[5] Plan for ***evaluating relationship effectiveness*** (e.g., bi-annual review of mentorship meeting minutes, goals, and outcomes/accomplishments):
I will plan to meet with the individual members of my mentorship committee in person biannually to review and evaluate the effectiveness of our mentor/mentee relationship and to establish tangible goals for the following 6 months.

[6] ***Relationship termination clause:*** In the event that either party finds the mentoring relationship unproductive and requests that it be terminated, we agree to honor that individual's decision without question or blame.

[7] ***Duration:*** This mentorship relationship will continue as long as both parties feel comfortable with its productivity or until: I have successfully competed for a non-mentored award.

Mentee's Signature [redacted] Mentor's Signature [redacted] Date 1/28/19

Mentorship Agreement

[1] ***Goals*** (what you hope to achieve as a result of this relationship; e.g., gain perspective relative to skills necessary for success in academia, explore new career opportunities/alternatives, obtain knowledge of organizational culture, networking, leadership skill development, etc.):
My goal is to acquire the skillset neeeded to succeed in academic medicine as a clinician-scientist by continuing to build my fund of knowledge, exploring new methods to scientifically approach clinical challenges, and by strengthening my grant writing skills. My immediate goal is to gain support as a Roadmap Scholar.

[2] ***Steps to achieving goals*** as stated above (e.g., meeting regularly, manuscripts/grants, collaborating on research projects, steps to achieving independence, etc.):
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