Pulmonary Medicine

Division Details

RESEARCH AND TRAINING DETAILS	
Faculty	**28**
Joint Appointment Faculty	**8**
Research Fellows and Post Docs	**12**
Research Graduate Students	**2**
Total Annual Grant Award Dollars	**$6,558,063**
Total Annual Industry Award Dollars	**$1,413,330**
Total Publications	**95**

CLINICAL ACTIVITIES AND TRAINING	
Clinical Fellows	**12**
Inpatient Encounters	**11,492**
Outpatient Encounters	**22,233**

Row 1: J Crisalli, N Simakajornboon, B Chini, L Burns, R Amin, E Kramer, R Szczesniak, J Woods, M Schecter, N Gurbani

Row 2: S Durrani, T Dye, E Hysinger, H Sawnani, J Clancy, C Towe, A Ziady, A Naren, W Hardie, D Grossoehme, M Seid, R Wood

Research Highlights

The Center for Pulmonary Imaging Research-Neonatal Imaging Highlights

The Center for Pulmonary Imaging Research (CPIR), established in 2013 under the leadership of Dr. Jason Woods, PhD, has a mission to broaden the understanding of regional lung structure and function, and of how these are altered by pulmonary disease. A primary research focus of the CPIR includes neonatal pulmonary imaging using a unique, neonatal-sized MRI scanner sited within the NICU. Recent work on imaging infants with bronchopulmonary dysplasia (BPD) has demonstrated that lung MRI is able to spatially resolve and quantify structural abnormalities in neonatal lung tissue with CT-like resolution and density, but without the ionizing radiation associated with CT. Dr Woods and his team has used MRI results in BPD patients to differentiate subtle differences between mild and more severe disease, through analysis of lung parenchyma that is outside of the normal range and can represent either fibrosis or alveolar simplification. These findings may serve as a basis for defining individual phenotypes of disease, which could impact clinical care and predict future outcomes. In addition, recent developments on a novel MRI acquisition sequence (called ultrashort echo time MRI) and associated image reconstruction methods have demonstrated the ability to generate images gated to various phases of respiration. This also allows inspiration-expiration differences to be examined, but also allows data acquired during motion-corrupted periods to be discarded, while preserving data acquired during periods of quiescence. Preliminary implementation of these techniques has shown promise in visualizing rare neonatal lung disorders (such as congenital diaphragmatic hernia or tracheal esophageal fistula/esophageal atresia) both before and after surgical repair. Monitoring and quantification of lung and airway tissues at pre- and post-repair time-points will provide important, new insights into patients' recovery trajectories.

Developing a Learning Network for Cystic Fibrosis

Imagine a system of cystic fibrosis (CF) care that can produce these outcomes: The average patient health-related quality of life is no different from that of the general population, people with CF and their families are able to achieve their stated goals, and the median age at death has doubled from 27.5 years (2013 data) to 55 years. What will it take to get there? To answer this question, a team led by Michael Seid, PhD, has received funding from the Cystic Fibrosis Foundation to design and develop the CF care model of the future. This team envisions a system that makes it easier for everyone-families, people with CF, clinicians, researchers and others-to work together at scale to improve health, care and costs for people with CF. This builds on improvement work at Cincinnati Children's Cystic Fibrosis Center, the CF Foundation's work in developing a patient registry and care center network, and the James M. Anderson Center for Health Systems Excellence development of learning networks in other conditions. Beginning with 13 adult and pediatric programs, the pilot CF Learning Network will develop the social, technical and scientific infrastructure for collaborative learning and improvement; and improve outcomes such as quality of life, patients' ability to meet their personal goals and clinician joy in work. If successful, the CF Foundation plans to spread the CF Learning Network to CF clinical programs throughout the country

Significant Publications

Walkup LL, Tkach JA, Higano NS, Thomen RP, Fain SB, Merhar SL, Fleck RJ, Amin RS, **Woods JC**. **Quantitative Magnetic Resonance Imaging of Bronchopulmonary Dysplasia in the Neonatal Intensive Care Unit Environment**. *Am J Respir Crit Care Med*. 2015 Nov 15;192(10):1215-22.

In this pilot study, the research team demonstrated the feasibility of the use of a small footprint MRI scanner in the neonatal intensive care unit. Pulmonary MRI revealed quantifiable, significant differences between patients with bronchopulmonary dysplasia, premature patients without BPD, and full-term control subjects. Researchers could implement these methods individually phenotype disease, which may impact clinical care and predict future outcomes.

Clancy JP, Davis SD, Ratjen F, Brumback LC, Johnson RC, Filbrun AG, Kerby GS, Panitch HB, Donaldson SH, Rosenfeld M. **Infant lung function tests as endpoints in the ISIS multicenter clinical trial in cystic fibrosis**. *J Cyst Fibros*. 2016 May;15(3):386-91.

In this study, the team demonstrated that infant pulmonary function tests are not appropriate primary endpoints for multicenter clinical trials due to challenges of obtaining acceptable data and near-normal average raised volume measurements. The results indicated that raised volume measures have potential to serve as secondary endpoints in future clinical CF trials in young children with CF.

Shamsuzzaman AS, Somers VK, Knilans TK, Ackerman MJ, Wang Y, **Amin RS**. **Obstructive Sleep Apnea in Patients with Congenital Long QT Syndrome: Implications for Increased Risk of Sudden Cardiac Death**. *Sleep*. 2015 Jul;138(7):1113-9.

In this report, Amin and colleagues demonstrated that the presence and severity of obstructive sleep apnea (OSA) in patients with congenital long QT syndrome (LQTS) associates with increased QT prolongation corrected for heart rate. This is an important biomarker of sudden cardiac death (SCD). Treatment of OSA in LQTS patients may reduce QT prolongation, thus reducing the risk of LQT-triggered SCD.

Shaughnessy EE, White C, Shah SS, Hubbell B, Sucharew H, **Sawnani H**. **Implementation of Postoperative Respiratory Care for Pediatric Orthopedic Patients**. *Pediatrics*. 2015 136(2): e505-12.

Members of the research team implemented an innovative respiratory care algorithm in hip and spine surgery patients by empowering RTs and engaging families to participate in care. In this quality improvement-based algorithm, the investigators found that this approach associates with decreased prolonged oxygen use in patients with chronic underlying pulmonary conditions.

Sinha C, Ren A, **Arora K**, Moon CS, Yarlagadda S, Woodrooffe K, Lin S, Schuetz JD, **Ziady AG**, **Naren AP**. **PKA and actin play critical roles as downstream effectors in MRP4-mediated regulation of fibroblast migration**. *Cell Signal*. 2015 Jul;27(7):1345-55.

In this series of studies, the research team found that actin interacts with multidrug resistance protein MRP4 of fibroblasts, predominantly at the plasma membrane, and an intact actin cytoskeleton required to restrict MRP4 to specific microdomains. Increased accumulation of cAMP in Mrp4(-/-) fibroblasts facilitated cortical actin polymerization in a PKA-dependent manner at the fibroblast leading edge, which in turn increased the overall rate of cell migration to accelerate the process of wound healing.

Together, the findings from this study suggest a novel cAMP-dependent mechanism for MRP4-mediated regulation of fibroblast migration whereby PKA and actin play critical roles as downstream effectors in wound healing.

Division Publications

1. Adams DM, Trenor CC, 3rd, Hammill AM, Vinks AA, Patel MN, Chaudry G, Wentzel MS, Mobberley-Schuman PS, Campbell LM, Brookbank C, Gupta A, Chute C, Eile J, McKenna J, Merrow AC, Fei L, Hornung L, Seid M, Dasgupta AR, Dickie BH, et al. **Efficacy and Safety of Sirolimus in the Treatment of Complicated Vascular Anomalies.** *Pediatrics*. 2016; 137:e20153257.
2. Amin RS, Rutter MJ. **Airway Disease and Management in Bronchopulmonary Dysplasia.** *Clin Perinatol*. 2015; 42:857-70.
3. Arora K, Naren A. **Pharmacological Correction of Cystic Fibrosis: Molecular Mechanisms at the Plasma Membrane to Augment Mutant Cftr Function.** *Curr Drug Targets*. 2016; 17:1275-81.
4. Arora K, Sinha C, Zhang W, Moon C, Ren A, Yarlagadda S, Dostmann W, Adebiyi A, Haberman Y, Denson L. **Altered Cgmp Dynamics at the Plasma Membrane Contribute to Diarrhea in Ulcerative Colitis.** *Am J Pathol*. 2015; 185:2790-804.
5. Arora K, Yarlagadda S, Zhang W, Moon C, Bouquet E, Srinivasan S, Li C, Stokes D, Naren A. **Personalized Medicine in Cystic Fibrosis: Genistein Supplementation as a Treatment Option for Patients with a Rare S1045y-Cftr Mutation.** *Am J Physiol*. 2016; 311:L364-74.
6. Bacharier L, Guilbert T, Mauger D, Boehmer S, Beigelman A, Fitzpatrick A, Jackson D, Baxi S, Benson M, Burnham C-A. **Early Administration of Azithromycin and Prevention of Severe Lower Respiratory Tract Illnesses in Preschool Children with a History of Such Illnesses a Randomized Clinical Trial.** *JAMA*. 2015; 314:2034-44.
7. Bacharier LB, Guilbert TW, Martinez FD. **Early Azithromycin Treatment to Prevent Severe Lower Respiratory Tract Illnesses in Children--Reply.** *JAMA*. 2016; 315:2122-3.
8. Balogh A, Shimizu Y, Lee S, Norman D, Gangwar R, Bavaria M, Moon C, Shukla P, Rao R, Ray R. **The Autotaxin-Lpa(2) Gpcr Axis Is Modulated by Gamma-Irradiation and Facilitates DNA Damage Repair.** *Cell Signal*. 2015; 27:1751-62.
9. Basil JS, Santoro SL, Martin LJ, Healy KW, Chini BA, Saal HM. **Retrospective Study of Obesity in Children with Down Syndrome.** *J Pediatr*. 2016; 173:143-8.
10. Beigelman A, Durrani S, Guilbert T. **Should a Preschool Child with Acute Episodic Wheeze Be Treated with Oral Corticosteroids? A Pro/Con Debate.** *J Allergy Clin Immunol Pract*. 2016; 4:27-35.
11. Boat T, Buka S, Perrin J. **Children with Mental Disorders Who Receive Disability Benefits a Report from the Iom.** *JAMA*. 2015; 314:2019-20.
12. Brewington J, Clancy JP. **Diagnostic Testing in Cystic Fibrosis.** *Clin Chest Med*. 2016; 37:31-46.
13. Brewington JJ, McPhail GL, Clancy JP. **Lumacaftor Alone and Combined with Ivacaftor: Preclinical and Clinical Trial Experience of F508del Cftr Correction.** *Expert Rev Respir Med*. 2016; 10:5-17.
14. Buggio M, Towe C, Annan A, Kaliberov S, Lu ZH, Stephens C, Arbeit JM, Curiel DT. **Pulmonary Vasculature Directed Adenovirus Increases Epithelial Lining Fluid Alpha-1 Antitrypsin Levels.** *J Gene Med*. 2016; 18:38-44.
15. Chervin RD, Ellenberg SS, Hou X, Marcus CL, Garetz SL, Katz ES, Hodges EK, Mitchell RB, Jones DT, Arens R, Amin R, Redline S, Rosen CL, Childhood Adenotonsillectomy Trial. **Prognosis for Spontaneous Resolution of Osa in Children.** *Chest*. 2015; 148:1204-13.
16. Chirkova T, Lin S, Oomens A, Gaston K, Boyoglu-Barnum S, Meng J, Stobart C, Cotton C, Hartert T, Moore M. **Cx3cr1 Is an Important Surface Molecule for Respiratory Syncytial Virus Infection in Human Airway Epithelial Cells.** *J Gen Virol*. 2015; 96:2543-56.

17. Clancy JP. **Cystic Fibrosis Transmembrane Conductance Regulator Function in Airway Smooth Muscle. A Novel Role in Cystic Fibrosis Airway Obstruction.** *Am J Respir Crit Care Med*. 2016; 193:352-3.

18. Davis S, Ratjen F, Brumback L, Johnson R, Filbrun A, Kerby G, Panitch H, Donaldson S, Rosenfeld M, Davis S. **Infant Lung Function Tests as Endpoints in the Isis Multicenter Clinical Trial in Cystic Fibrosis.** *J Cyst Fibros*. 2016; 15:386-91.

19. Dell M, Grossoehme D. **Spritual and Relgious Considerations**. In: L Wiener, M Pao, A Kazaket al, eds. *Quick Reference for Pediatric Oncology Clinicians: The Psychiatric and Psychological Dimensions of Pediatric Cancer Symptom Management, Second Edition*. New York: Oxford University Press; 2015:281-90.

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21. Downes KJ, Patil NR, Rao MB, Koralkar R, Harris WT, Clancy JP, Goldstein SL, Askenazi DJ. **Risk Factors for Acute Kidney Injury During Aminoglycoside Therapy in Patients with Cystic Fibrosis.** *Pediatr Nephrol*. 2015; 30:1879-88.

22. Durrani S, Guilbert T. **Short- and Long-Term Efficacy of Prednisolone for First Acute Rhinovirus-Induced Wheezing Episode**. In: M Cabana, ed. *Year Book of Pediatrics 2016*. New York: Elsevier; 2015:403-07.

23. Dye T, Jain S, Simakajornboon N. **Outcomes of Long-Term Iron Supplementation in Pediatric Restless Legs Syndrome/Periodic Limb Movement Disorder (Rls/Plmd).** *Sleep Medicine*. 2015.

24. Ehsan Z, Clancy J. **Management of Pseudomonas Aeruginosa Infection in Cystic Fibrosis Patients Using Inhaled Antibiotics with a Focus on Nebulized Liposomal Amikacin.** *Future Microbiology*. 2015; 10:1901-12.

25. Ehsan Z, Mahmoud M, Shott SR, Amin RS, Ishman SL. **The Effects of Anesthesia and Opioids on the Upper Airway: A Systematic Review.** *Laryngoscope*. 2016; 126:270-84.

26. Ehsan Z, Nathan JD, Kercsmar CM. **An Infant with a Hyperlucent Chest Mass: An Unexpected Diagnosis.** *Pediatr Pulmonol*. 2015; 50:E52-4.

27. Flume PA, Clancy JP, Retsch-Bogart GZ, Tullis DE, Bresnik M, Derchak PA, Lewis SA, Ramsey BW. **Continuous Alternating Inhaled Antibiotics for Chronic Pseudomonal Infection in Cystic Fibrosis.** *J Cyst Fibros*. 2016.

28. Gerald J, Gerald L, Vasquez M, Morgan W, Boehmer S, Lemanske R, Mauger D, Strunk R, Szefler S, Zeiger R. **Markers of Differential Response to Inhaled Corticosteroid Treatment among Children with Mild Persistent Asthma.** *J Allergy Clin Immunol Pract.* 2015; 3:540.

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31. Grossoehme D. **'God Tells the Doctors to Pick the Right Medicine' - Leeann, a 12-Year-Old with Cycstic Fibrosis**. In: S Nolan, G Fitchett, eds. *Spiritual Care in Practice: Case Studies in Healthcare Chaplaincy*. London: Jessica Kingsley Publishers; 2015:31-50.

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Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Raouf Samy Amin, MD	Passive Stretch of the Chest Wall in Patients with Congenital Muscular Dystrophy	Cure CMD	Cure CMD - Amin	5/3/2013 - 5/2/2016	$40,000
Raouf Samy Amin, MD	Impact of Treatment of Mild Sleep-Disordered Breathing on Children's Health	National Institutes of Health (Children's Hospital of Philadelphia)	U01 HL125295	9/4/2015 - 6/30/2020	$193,192
Kavisha Arora, PHD	Personalized Medicine-Elucidating Mechanism of a Novel CF Mutation	Cystic Fibrosis Foundation	ARORA16F0	3/1/2016 - 2/28/2018	$46,250
Lisa A Burns, MD	Transforming CF Care Through Shared Decision Making	Cystic Fibrosis Foundation (University of Cincinnati)	JOSEPH15QI0	1/1/2015 - 12/31/2017	$44,107
John Paul Clancy, MD	CFF-TDN site	Cystic Fibrosis Fdn	AMIN09Y0/CLANCY14Y0	1/1/2013 -	$96,688

		Therapeutics, Inc		12/31/2016	
John Paul Clancy, MD	CFFT Biomarkers Consortium	Cystic Fibrosis Fdn Therapeutics, Inc	CLANCY11CS0	1/1/2011 - 12/31/2015	$46,051
John Paul Clancy, MD	PROSPECT	Cystic Fibrosis Fdn Therapeutics, Inc	CLANCY14K1	7/1/2014 - 6/30/2019	$108,731
John Paul Clancy, MD	Pilot Development of Translational Primary Human Airway	Cystic Fibrosis Foundation	CLANCY14XX0	7/1/2014 - 6/30/2017	$95,256
John Paul Clancy, MD	Upper and Lower Airway CF Microbiome: Pediatric Subject Characterization, Sample, Acquisition and Processing	Cystic Fibrosis Fdn Therapeutics, Inc	CLANCY14XX1	7/1/2014 - 6/30/2016	$26,051
John Paul Clancy, MD	TDC ARC Award	Cystic Fibrosis Fdn Therapeutics, Inc	CLANCY14Y4	12/1/2014 - 11/30/2016	$77,153
John Paul Clancy, MD	Personalizing Cystic Fibrosis Research Translation	Cystic Fibrosis Foundation	CLANCY15R0	7/1/2015 - 6/30/2019	$470,000
John Paul Clancy, MD	TDN Steering Committee Chair	Cystic Fibrosis Fdn Therapeutics, Inc	CLANCY16Y3	1/1/2016 - 12/31/2018	$23,138
John Paul Clancy, MD	MR Predictors of Infection, Inflammation, and Structural Lung Damage in CF	National Institutes of Health	R01 HL116226	9/26/2012 - 6/30/2017	$482,554
Zackary Cleveland, PHD	Regional Biomarkers of Peripheral Lung Disease in Cystic Fibrosis	Cystic Fibrosis Fdn Therapeutics, Inc	CLEVEL16A0	4/1/2016 - 3/31/2019	$108,000
Zackary Cleveland, PHD	Time-Resolved 129Xe Ventilation-Perfusion MRI in Models	National Institutes of Health	R00 HL111217	8/15/2015 - 7/31/2018	$248,999
Daniel Grossoehme D.Min.	Training Research-Literate Chaplains as Ambassadors for Spirituality and Health	John Templeton Foundation (Rush Medical University Center)	51996	7/1/2015 - 6/30/2017	$8,911
William D Hardie, MD John Paul Clancy, MD	Cincinnati Children's Summer Medical Student Respiratory Research Fellowship	National Institutes of Health	T35 HL113229	5/1/2016 - 4/30/2021	$68,526
James E Heubi, MD	Infant Nutrition Study	Cystic Fibrosis Fdn Therapeutics, Inc (Seattle Children's)	BONUS11K0	12/1/2010 - 4/30/2016	$7,805

Elizabeth Kramer	First and Second Year Clinical Fellowship Grant	Cystic Fibrosis Foundation	KRAMER14B0	7/1/2014 - 6/30/2016	$66,250
Satish K Madala, PHD	Molecular Mechanisms of TGF (alpha)-Driven Pulmonary Fibrosis	Parker B. Francis Fellowship Program	Madala - PBF	7/1/2013 - 6/30/2016	$54,000
Gary McPhail, MD	Cystic Fibrosis Center Program Accreditation And Funding	Cystic Fibrosis Foundation	CC160-130	7/1/2013 - 6/30/2018	$144,651
Gary McPhail, MD	Implementation of the Depression & Anxiety Guidelines	Cystic Fibrosis Foundation	CMHC160-15	1/1/2016 - 12/31/2018	$53,246
Gary McPhail, MD	CFF Success with Therapies Research Consortium - CCHMC	Cystic Fibrosis Fdn Therapeutics, Inc	MCPHAI14PE0	8/1/2014 - 7/31/2017	$27,000
Anjaparavanda Naren, PHD	CF-Patient Specific Enteroids from Small Intestine and Colon	Cystic Fibrosis Fdn Therapeutics, Inc	NAREN14XX0	7/1/2014 - 6/30/2017	$223,357
Anjaparavanda Naren, PHD	Inhibition of an Apical cAMP/cGMP transporter (MRP4) in the Gut induces Diarrhea	National Institutes of Health	R01 DK080834	9/18/2013 - 3/31/2018	$333,536
Anjaparavanda Naren, PHD	LPA2 Receptor-containing Complexes in Regulating Secretory Diarrhea	National Institutes of Health	R01 DK093045	7/1/2015 - 6/30/2020	$351,000
Anjaparavanda Naren, PHD	Characterization of an Inhibitory Protein Complex for Cystic Fibrosis Therapy	National Institutes of Health (Univ of Tennessee Health Science Center)	R01 HL123535	8/15/2014 - 6/30/2019	$17,539
Kai Ruppert, PHD	Simultaneous Xe129 MRI of Regional Lung Ventilation and Gas Uptake in COPD	National Institutes of Health (University of Virginia)	R01 HL109618	12/23/2013 - 5/31/2016	$19,188
Michael Seid, PHD	Enabling Uptake of a Registry-Supported Care and Learning System in the U.S.	Robert Wood Johnson Foundation (Trustees of Dartmouth)	72313	12/15/2014 - 12/14/2017	$401,775
Michael Seid, PHD	Measures of Hypoglycemia and Glycemic Variability Using Continuous Glucose Monitoring in the FL3X Intervention for Youth with Type 1 Diabetes	The Leona M & Harry B Helmsley Charitabl (University of North Carolina)	2014PG-T1D030	1/1/2014 - 12/31/2016	$10,400

Michael Seid, PHD	A C3N for CF: Design and Development of a Peer-Produced Learning Health System	Cystic Fibrosis Fdn Therapeutics, Inc	SEID14A0	7/1/2014 - 12/31/2015	$277,355
Michael Seid, PHD	A CF C3N Care Model of the Future: Proposal for Piloting a Learning Health System	Cystic Fibrosis Fdn Therapeutics, Inc	SEID15A0	1/1/2016 - 12/31/2018	$800,488
Michael Seid, PHD	FL3X: An Adaptive Intervention to Improve Outcomes for Youth with Type 1 Diabetes	National Institutes of Health (University of North Carolina)	UC4 DK101132	9/15/2013 - 6/30/2018	$629,017
Jason C Woods, PHD	Pathogenesis-Driven Therapeutic Develoment for Pulmonary Alveolar Microlithiasis	National Institutes of Health (University of Cincinnati)	R01 HL127455	4/1/2015 - 3/31/2020	$70,636
Jason C Woods, PHD John Paul Clancy, MD	UTE MRI to Monitor CF Lung Disease and Response to CFTR	National Institutes of Health	R01 HL131012	5/1/2016 - 3/31/2021	$760,483
Jason C Woods, PHD	Severe Asthma Research Program	National Institutes of Health (Washington University)	U10 HL109257	2/1/2013 - 5/31/2017	$8,547
Sara M Zak, MD	First & Second Year Clinical Fellowship	Cystic Fibrosis Foundation	ZAK15B0	7/1/2015 - 6/30/2017	$61,250
Assem Ziady, PHD	Dysregulation of Nrf2 in CF Epithelia	National Institutes of Health	R01 HL109362	4/22/2015 - 4/30/2016	$56,933
Total Annual Grant Award Dollars					**$6,558,063**

Annual Industry Award Dollars

Investigator	Industry Sponsor	Amount
John Paul Clancy, MD	Eccrine	$10,000
John Paul Clancy, MD	Nivalis Therapeutics	$209,762
John Paul Clancy, MD	ProQR Therapeutics N.V.	$576,112
Daniel Grossoehme, DMin	Ipsos Insight, LLC	$34,615
Gary McPhail, MD	Parion Services, Inc.	$137,420
Gary McPhail, MD	Vertex Pharmaceutical Incorporated	$82,381
Anjaparavanda Naren, PHD	Ironwood Pharmaceuticals, Inc.	$229,921
Assem Ziady, PHD	Gilead Sciences, Inc.	$66,650
Assem Ziady, PHD	Nivalis Therapeutics	$66,470

Total Annual Industry Award Dollars	**$1,413,330**