Department of Pediatrics
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

2018 Annual Report
Division of Pulmonology and Sleep Medicine

DIVISION DESCRIPTION

The Division of Pediatric Pulmonology and Sleep Medicine provides interdisciplinary family-centered care for children with respiratory disorders, including asthma, cystic fibrosis, sleep disorders, neuromuscular disorders, and chronic lung disease.

The division continues to build upon leading-edge clinical research into the early diagnosis and epidemiology of cystic fibrosis with new investigations into the disease's microbiome. Additional clinical research focuses on environment-disease interactions in asthma, pulmonary management of children with neuromuscular disorders, education and effect of sleep disorders in children. The division also has an active translational research program that is investigating the role of stem and progenitor cells in newborn lung disease. Finally, we host one of two pediatric sleep medicine programs in Wisconsin.

2018 HIGHLIGHTS

- **Vivek Balasubramaniam, MD,** received one of 12 grants awarded nationally by The Hartwell Foundation as part of its 2017 Hartwell Individual Biomedical Research Award competition. He received recognition as a Hartwell Investigator, along with three years and $300,000 of support for his project, "Application of Cellular-Derived Therapies for the Regeneration of Lung Structure and Function." This project aims to determine the specific components and mechanisms of innovative use of extracellular vesicles (EVs) in the treatment of bronchopulmonary dysplasia (BPD) in an animal model, so that investigators can develop new innovative therapies to cure lung diseases of prematurity.

  Dr. Balasubramaniam and Kim Whitmore, PhD, RN (Nursing) also received $48,000 in funding from the UW Foundation for their project, "eHomeCare - An Innovative Health Care Delivery Support System for Homecare Nurses." This project aims to increase access to an evidence-based, nursing-driven educational program, which provides homecare nurses with comprehensive information about the care of children with a tracheostomy and/or ventilator.

- In 2018, *U.S. News and World Report* ranked UW Health's American Family Children's Hospital in the top 50 children's hospitals for pulmonology.

RECENT PUBLICATIONS

Belter L, Cook SF, Crawford TO, Jarecki J, Jones CC, Kissel JT, **Schroth M**, Hobby K. An overview of the Cure SMA membership database: Highlights of key demographic and clinical characteristics of SMA members. *J Neuromuscul Dis*. 2018;5(2):167-176. doi: 10.3233/JND-170292. PubMed PMID: 29614694; PubMed Central PMCID: PMC6004903.

Braun RK, **Chetty C**, **Balasubramaniam V**, Centanni R, Haraldsdottir K, Hematti P, Eldridge MW. Intraperitoneal injection of MSC-derived exosomes prevent experimental bronchopulmonary dysplasia. *Biochem Biophys Res Commun*. 2018 Sep 18;503(4):2653-2658. doi: 10.1016/j.bbrc.2018.08.019. Epub 2018 Aug 7. PubMed PMID: 30093115.

Bristol JA, Djavadian R, Albright ER, Coleman CB, Ohashi M, Hayes M, Romero-Masters JC, Barlow EA, **Farrell PM**, Rochford R, Kalejta RF, Johannsen EC, Kenney SC. A cancer-associated Epstein-Barr virus BZLF1 promoter variant enhances lytic infection. *PLoS Pathog*. 2018 Jul 27;14(7):e1007179. doi: 10.1371/journal.ppat.1007179. eCollection 2018 Jul. PubMed PMID: 30052684; PubMed Central PMCID: PMC6082571

Farrell P, Férec C, Macek M, Frischer T, Renner S, Riss K, Barton D, Repetto T, Tzetis M, Giteau K, Duno M, Rogers M, Levy H, Sahbatou M, Fichou Y, Le Maréchal C, Génin E. Estimating the age of p.(Phe508del) with family studies of geographically distinct European populations and the early spread of cystic fibrosis. *Eur J Hum Genet*. 2018 Dec;26(12):1832-1839. doi: 10.1038/s41431-018-0234-z. Epub 2018 Aug 8. PubMed PMID: 30089827; PubMed Central PMCID: PMC6244163.

Finkel RS, Mercuri E, Meyer OH, Simonds AK, **Schroth MK**, Graham RJ, Kirschner J, Iannaccone ST, Crawford TO, Woods S, Muntoni F, Wirth B, Montes J, Main M, Mazzone ES, Vitale M, Snyder B, Quijano-Roy S, Bertini E, Davis RH, Qian Y, Sejersen T; SMA Care group. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. *Neuromuscul Disord*. 2018 Mar;28(3):197-207. doi: 10.1016/j.nmd.2017.11.004. Epub 2017 Nov 23. PubMed PMID: 29305137. **

Krosschell KJ, Kissel JT, Townsend EL, Simeone SD, Zhang RZ, Reyna SP, Crawford TO, **Schroth MK**, Acsadi G, Kishnani PS, Von Kleist-Retzow JC, Hero B, D'Anjou G, Smith EC, Elsheikh B, Simard LR, Prior TW, Scott CB, Lasalle B, Sakonju A, Wirth B, Swoboda KJ; Project Cure SMA Investigator's Network. Clinical trial of L-Carnitine and valproic acid in spinal muscular atrophy type I. *Muscle Nerve*. 2018 Feb;57(2):193-199. doi: 10.1002/mus.25776. Epub 2017 Sep 18. PubMed PMID: 28833236.

LeGrys VA, Moon TC, Laux J, **Rock MJ**, Accurso F. Analytical and biological variation in repeated sweat chloride concentrations in clinical trials for CFTR modulator therapy. *J Cyst Fibros*. 2018 Jan;17(1):43-49. doi: 10.1016/j.jcf.2017.07.008. Epub 2017 Jul 22. PubMed PMID: 28739209.

Lewis KJR, Hall JK, Kiyotake EA, Christensen T, **Balasubramaniam V**, Anseth KS. Epithelial-mesenchymal crosstalk influences cellular behavior in a 3D alveolus-fibroblast model system. *Biomaterials*. 2018 Feb;155:124-134. doi: 10.1016/j.biomaterials.2017.11.008. Epub 2017 Nov 15. PubMed PMID: 29175081; PubMed Central PMCID: PMC5748390.

Mercuri E, Finkel RS, Muntoni F, Wirth B, Montes J, Main M, Mazzone ES, Vitale M, Snyder B, Quijano-Roy S, Bertini E, Davis RH, Meyer OH, Simonds AK, **Schroth MK**, Graham RJ, Kirschner J, Iannaccone ST, Crawford TO, Woods S, Qian Y, Sejersen T; SMA Care Group. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. *Neuromuscul Disord*. 2018 Feb;28(2):103-115. doi: 10.1016/j.nmd.2017.11.005. Epub 2017 Nov 23. PubMed PMID: 29290580. **

Meyerholz DK, Stoltz DA, Gansemer ND, Ernst SE, Cook DP, Strub MD, LeClair EN, **Barker CK**, Adam RJ, Leidinger MR, Gibson-Corley KN, Karp PH, Welsh MJ, McCray PB Jr. Lack of cystic fibrosis transmembrane conductance regulator disrupts fetal airway development in pigs. *Lab Invest*. 2018 Jun;98(6):825-838. doi: 10.1038/s41374-018-0026-7. Epub 2018 Feb 21. PubMed PMID: 29467455; PubMed Central PMCID: PMC6019641.

Sagel SD, Khan U, Jain R, Graff G, Daines CL, Dunitz JM, Borowitz D, Orenstein DM, Abdulhamid I, Noe J, Clancy JP, Slovis B, **Rock MJ**, McCoy KS, Strausbaugh S, Livingston FR, Papas KA, Shaffer ML. Effects of an antioxidant-enriched multivitamin in cystic fibrosis. A randomized, controlled, multicenter clinical trial. *Am J Respir Crit Care Med*. 2018 Sep 1;198(5):639-647. doi: 10.1164/rccm.201801-0105OC. PubMed PMID: 29688760; PubMed Central PMCID: PMC6118015.

Sanders DB, Li Z, Parker-McGill K, **Farrell P**, Brody AS. Quantitative chest computerized tomography and FEV(1) equally identify pulmonary exacerbation risk in children with cystic fibrosis. *Pediatr Pulmonol*. 2018 Oct;53(10):1369-1377. doi: 10.1002/ppul.24144. Epub 2018 Aug 29. PubMed PMID: 30160050.

Sanders DB, Zhang Z, **Farrell PM**, Lai HJ; Wisconsin CF Neonatal Screening Group. Early life growth patterns persist for 12 years and impact pulmonary outcomes in cystic fibrosis. *J Cyst Fibros*. 2018 Jul;17(4):528-535. doi: 10.1016/j.jcf.2018.01.006. Epub 2018 Feb 1. PubMed PMID: 29396025; PubMed Central PMCID: PMC6026029.

Shah S, **Balasubramaniam V**, Brumberg HL, Sanders L. Policy priorities for child health: results from a membership survey of the Society for Pediatric Research. *Pediatr Res*. 2018 Jul;84(1):6-9. doi: 10.1038/s41390-018-0034-8. Epub 2018 Jun 18. PubMed PMID: 29915410.

**ePub only; no print citation available when report was compiled*
*** Publication had previously appeared in 2017 report as an ePub*

GRANT SUPPORT

Principal Investigator	Sponsor	Title	Co-Investigators
Balasubramaniam, Vivek	Health Resources & Services Administration (HRSA)	UW pediatric pulmonary center	Pulmonology: Carrie Barker, Camille Matthews, Michael Rock
Balasubramaniam, Vivek	The Hartwell Foundation	Application of cellular-derived therapies for the regeneration of lung structure and function	Critical Care: Marlowe Eldridge (Collaborator)
Farrell, Philip M	Legacy of Angels	Assessing the added value of whole genome sequencing in cystic fibrosis newborn screening	Genetics: Mei Baker
Lai, Huichuan J	National Institutes of Health (NIH)	Early childhood diet, growth, gut microbiome and lung health in cystic fibrosis	Pulmonology: Michael Rock, Philip Farrell
Lai, Huichuan J	Cystic Fibrosis Foundation Therapeutics	Impact of early malnutrition on lung disease development in cystic fibrosis	Pulmonology: Michael Rock, Philip Farrell

Lai, Huichuan J	National Institutes of Health (NIH) & Emory University	Method development of survival dynamic regression in chronic disease research	
Jones, Stephanie G (UW Department of Psychiatry)	National Institutes of Health (NIH)	Local sleep loss and neurobehavioral function in pediatric sleep-disordered breathing: a high density EEG investigation	Pulmonology: Cami Matthews
Rock, Michael J	Children's Hospital and Regional Medical Center	EPIC-002	
Rock, Michael J	Children's Hospital and Regional Medical Center	EPIC-001: Efficacy and safety of intermittent antimicrobial therapy for the treatment of the new onset pseudomona s aeruginosa airway infection in young patients with cystic fibrosis	
Rock, Michael J	Cystic Fibrosis Foundation Therapeutics & Seattle Children's Hospital	CFFC-OB-11	
Rock, Michael J	Cystic Fibrosis Foundation Therapeutics	ARC (additional research coordinator award)	
Rock, Michael J	Vertex Pharmaceuticals, Inc.	VX15-809-110: A phase 3, rollover study to evaluate the safety and efficacy of long-term treatment with lumacaftor in combination with ivacaftor in subjects aged 6 years and older with cystic fibrosis, homozygous for the F508del-CFTR mutation	
Rock, Michael J	Cystic Fibrosis Foundation	Clinical fellowship	

Rock, Michael J	Vertex Pharmaceuticals, Inc.	VX15-770-124: A phase 3, 2-part, open-label study to evaluate the safety, pharmacokinetics, and pharmacodynamics of ivacaftor in subjects with cystic fibrosis who are <24 months of age at treatment initiation and have a CFTR gating mutation	
Rock, Michael J	Cystic Fibrosis Foundation	CF center	
Rock, Michael J	Vertex Pharmaceuticals, Inc.	A phase 3, 2-arm, open-label study to evaluate the safety and pharmacodynamics of long-term ivacaftor treatment in subjects with cystic fibrosis who are less than 24 months of age at treatment initiation and have a CFTR gating mutation	
Rock, Michael J	Wisconsin Department of Health Services	Congenital disorders	
Rock, Michael J	Cystic Fibrosis Foundation Therapeutics	Therapeutics development center	
Rock, Michael J	Cystic Fibrosis Foundation Therapeutics & Seattle Children's Hospital	Characterizing CFTR modulated changes in sweat chloride & clinical outcomes	
Rock, Michael J	Vertex Pharmaceuticals, Inc.	A phase 3, 2-part, open-label study to evaluate the safety and pharmacokinetics of lumacaftor/ivacaftor in subjects 1 to less than 2 years of age with cystic fibrosis, homozygous for F508del	
Schroth, Mary/Schultz, Meredith	Muscular Dystrophy Association, Inc.	University of Wisconsin/AFCH MDA care center	