

BIOGRAPHICAL SKETCH

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NAME Scott H. Randell		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) Scott_Randell			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
State University of NY College at New Paltz	BS	1979	Biology
The Johns Hopkins University, Baltimore, MD	Ph.D.	1985	Toxicology/Experimental Pathology

A. Personal Statement

Research in my lab is currently focused on five areas where a greater knowledge of basic cell biology can be applied towards overcoming clinical lung disease problems.

- 1) *Identification of Airway Epithelial Stem Cells.* Our goals are to identify and isolate airway epithelial stem cells and to understand molecular mechanisms regulating airway epithelial cell proliferation and fate.
- 2) *Micro RNA Regulation of Human Airway Epithelial Phenotype- ARRA Award.* We will comprehensively determine the miRNA repertoire of human airway epithelial cells and will test the ability of miRNAs to alter cell structure and function.
- 3) *Innate Immunity in the Airway.* Our goals are to better understand airway epithelial adaptation to chronic injury and infection and to understand the relationship of adaptation to the pathogenesis of airway disease.
- 4) *Post-lung Transplant Ischemia Reperfusion Injury and Bronchiolitis Obliterans Syndrome.* We are examining mechanisms of lung injury relevant to transplantation and bronchiolitis obliterans syndrome, the leading cause of lung allograft failure.
- 5) *UNC CF Center Tissue Procurement and Cell Culture Core.* This Core provides primary and passaged human airway and alveolar epithelial cells, lung microvascular endothelial cells, media and expertise to UNC CF Center investigators and collaborators. This facility is a nationally and internationally recognized resource whose services are sought for collaboration, contract research, and training by academics, non-profit organizations, biotech and the pharmaceutical industry.

B. Positions and Honors, 1) Research and Professional Experience

1979-1981: Laboratory Associate, The Johns Hopkins University
 1981-1984: Medical Technologist, The Johns Hopkins Hospital
 1985-1989: Postdoctoral Fellow, Respiratory Medicine, Duke University Medical Center
 1989-1991: Staff Fellow, NIH/NIEHS
 1991-1994: Senior Staff Fellow, NIH/NIEHS
 1994-2005: Asst. Professor, Dept. of Medicine, University of North Carolina, Chapel Hill, NC
 2000-2005: Joint Appointment, Department of Cell and Molecular Physiology, UNC Chapel Hill
 2005-present: Assoc. Professor, Department of Cell and Molecular Physiology, UNC Chapel Hill
 2005-present: Joint Appointment, Dept. of Medicine, University of North Carolina, Chapel Hill, NC

2) Honors and Awards

1974-New York State Regents Scholarship, 1979-Graduate Cum Laude (B.S. Degree)
 1980-Scholarship from The Johns Hopkins University, 1981-Predoctoral Training Grant Recipient
 1985-Postdoctoral Training Grant Recipient

C. Selected Peer-Reviewed Publications (15 from more than 90).

- 1) **Randell SH**, Mercer RR, Young SL. Postnatal growth of pulmonary acini and alveoli in normal and oxygen-exposed rats studied by serial section reconstructions. *Am J Anat.* 1989 Sep;186(1):55-68. PMID: 2782288
- 2) **Randell SH**, Mercer RR, & Young SL. Neonatal hyperoxia alters the pulmonary alveolar and capillary structures of forty day old rats. *Am J Pathol* 136:1259-1266,1990. PMID: 2782288.
- 3) **Randell SH**, Silbajoris R, Young SL. Ontogeny of rat lung type II cells correlated with surfactant lipid and surfactant apoprotein expression. *Am J Physiol.* 1991 Jun;260(6 Pt 1):L562-70. PMID: 2058697
- 4) **Randell SH**, Comment C, Ramaekers FCS, & Nettesheim P. Properties of rat tracheal epithelial cells separated based on expression of cell surface α -galactosyl end groups. *Am J Respir Cell Mol Biol* 4:544-554,1991. PMID: 1711352.
- 5) **Randell SH**, Shimizu T, Ramaekers FCS & Nettesheim P. Expression of phenotypic markers during fetal and neonatal differentiation of rat tracheal epithelial cells. *Am J Respir Cell Mol Biol*, 8:546-555,1993. PMID: 7683198.
- 6) Liu JY, Nettesheim P & **Randell SH**. Growth and differentiation of tracheal progenitor cells. *Am J Physiol (Lung Cell Mol Physiol 10)*: L296-L307, 1994. PMID: 8166299.
- 7) Becker MN, Diamond G, Verghese MW & **Randell SH**. CD14-dependent LPS-induced β defensin 2 Expression in human tracheobronchial epithelium. *J Biol Chem*, 2000, 275:38, p.29731-29736. PMID: 10882713.
- 8) Borthwick DW, Shahbazian M, Krantz QT, Dorin JR & **Randell SH**. Evidence for Stem Cell Niches in the Murine Tracheal Epithelium. *Am J Respir Cell Mol Biol*, 2001, 24:662-670. PMID: 11415930.
- 9) Lundberg AS, **Randell SH**, Stewart SA, Elenbaas B, Hartwell KA, Brooks MW, Fleming MD, Olsen JC, Miller SW, Weinberg RA, Hahn WC. Immortalization and transformation of primary human airway epithelial cells by gene transfer. *Oncogene*. 2002 Jul 4; 21(29): 4577-86. PMID: 12085236
- 10) Becker MN, Sauer MS, Muhlebach M, Hirsh AJ, Wu Q, Verghese MW & **Randell SH**. Cytokine Secretion by Cystic Fibrosis Human Airway Epithelial Cells, *Am J Respir Crit Care Med*. 2004 Mar 1; 169(5): 645-53. PMID: 14670800.
- 11) Schoch KG, Lori A, Burns KA, Eldred T, Olsen JC & **Randell SH**. A Subset of Mouse Tracheal Epithelial Basal Cells Forms Large Colonies In Vitro. *Am J Physiol Lung Cell Mol Physiol*. 2004 Apr; 286(4): L631-42. PMID: 12959927.
- 12) Rawlins EL, Ostrowski LE, **Randell SH**, Hogan BL. Lung development and repair: Contribution of the ciliated lineage. *Proc Natl Acad Sci U S A*. 2007 Jan 9;104(2):410-7. PMID 17194755
- 13) Fulcher ML, Gabriel SE, Olsen JC, Livanos E, Tatreau JR, Saavedra MT, Salmon P, **Randell SH**. Novel Human Bronchial Epithelial Cell Lines For Cystic Fibrosis Research. *Am J Physiol Lung Cell Mol Physiol*. 2009 Jan;296(1):L82-91. Epub 2008 Oct 31. PMID: 18978040.
- 14) Livraghi A, Grubb BR, Hudson EJ, Wilkinson KJ, Sheehan JK, Mall MA, O'Neal WK, Boucher RC, & **Randell SH**. Airway and lung pathology due to mucosal surface dehydration in β -Epithelial Na⁺ Channel-overexpressing mice: role of TNF-alpha and IL-4R-alpha signaling, influence of neonatal development, and limited efficacy of glucocorticoid treatment. *J Immunol*. 2009 Apr 1;182(7):4357-67. PMID: 19299736.
- 15) Rock JR, Onaitis MW, Rawlins EL, Lu Y, Clark CP, Xue Y, **Randell SH**, Hogan BLM. Basal cells as stem cells of the mouse trachea and human airway epithelium. *Proc Natl Acad Sci U S A*. 2009 Aug 4;106(31):12771-5. Epub 2009 Jul 22. PMID: 19625615

D. Research Support

Ongoing Research Support

1 RC1 HL 100108 (Randell/Hammond/Hayes) 9/30/09-9/29/11
NIH/NHLBI

Micro RNA Regulation of Human Airway Epithelial Phenotype

The major goal of this project is to gain a comprehensive understanding of the miRNA repertoire and its expression and function in hBE cells. Role: Principal Investigator

1 RC1 ES 018686-01 (Superfine) 9/30/09-9/29/11
NIH/NHLBI

Computation and Cell Culture Models for Mucus Clearance

The goal of this project is to generate computations and cell culture based models for mucus clearance - these models will have the potential to act as a sensitive assay for environmental effectors that compromise mucus height regulation, mucus rheology, cilia density and coordination. Role: Principal Investigator

5 P30 DK 065988-06 Boucher (PI) 4/1/09-3/31/14

NIH/NIDDK

Molecular Therapy Core Center, Core F: Cell Culture Models Core- Provide novel airway epithelial culture systems, lung microvascular endothelial cells and hepatocytes. Role: Core Leader

5 P01 HL 034322-22 Boucher (PI) 2/1/07-1/31/12

NIH/NHLBI

Pulmonary Epithelia in Health and Disease, Core C: Cell Culture Core- Support PPG projects by performing the following functions: tissue procurement, cell isolation and culture, and genetic manipulation of cell cultures. Role: Core Leader

RANDEL07XX0 Randell (PI) 7/1/07-6/30/10

CFFT Inc.

NDRI-UNC-CFFT Cell Resource- Receive lung tissues, process for epithelial cell harvest, characterize the cells and distribute for CF research as designated by CFFT. Role: Principal Investigator

R026-CR07 (Boucher) 7/1/07-6/30/11

CFF

Epithelial Function in Cystic Fibrosis, Core C: Procure tissue, characterize patients, culture cells to support research projects, develop cell lines. Role: Core Leader

Subcontract on 5 R01 HL090146-02 Stripp (PI) 9/28/07-6/30/11

Duke University/NIH/NHLBI

Stem Cells to Enhance Bronchiolar Reparative Capacity- Procure and analyze human lung tissues and cells to assess functional activity of stem and progenitor cells. Role: Subcontract PI

1R01 HL 095396-01 Knowles/Wright (PI) 9/24/08-7/31/12*

NIH/NHLBI

Molecular Phenotypes for Cystic Fibrosis Lung Disease- Study the role of gene expression variation in CF lung disease and the integrated analysis of SNPs/CNVs and expression data. (*support starting yr 4) Role: Co-I

5 P01 HL 051818-15 (Samulski) 8/20/04-6/30/10*

NIH/NHLBI

Gene Therapy for Cystic Fibrosis, Core B: Tissue Procurement and Cell Culture

The goal of this Core is to provide human airway tissues and cells and media to PPG investigators. These basic services are distinct from, and do not overlap with, MTCC functions related to airway cells. *7/1/09-6/30/10 is a no-cost extension.

Subcontract 104163 (Karp) 7/1/08-6/30/10

Cincinnati Children's Hospital Medical Center (CCHMC)

(subcontract on Cystic Fibrosis Foundation grant R457-CR07, subcontract PI: Randell)

Research Development Program

The major goal of this subcontract is to provide services to the CCHMC RDP grant in isolating primary airway epithelial cells, harvesting cells, and culturing cells.

Pilot Project (Knowles) 5/1/09-4/30/10

UNC NC TRaCS Institute

Test New Drug (PTC124) to "Read-Through" Nonsense (STOP) Mutations and Correct Ciliary Function in Primary Ciliary Dyskinesia (PCD)

The major goal of this project is to test a currently available pharmacologic agent (PTC124; oral drug) in vitro as a potential treatment for nonsense (STOP) mutations in Primary Ciliary Cyskinesia (PCD), which is a recessive, genetically heterogeneous disorder of cilia.

Collaborative Funding Grant (Randell) 7/1/09-6/30/11
NC Biotech Center & Parion Sciences
The Development of Corneal and Conjunctival Epithelia Cultures for the Advancement of Novel Dry Eye Therapies

The major goals of this project are to develop primary human corneal and conjunctival epithelial cell cultures (1) to validate that ENaC plays a role in ocular fluid absorption in humans, and (2) for the development of a cell-based approach to study duration of action of multiple Parion compounds for the purpose of lead selection, with an ultimate goal of providing key insights into the biology underlying salt and fluid transport on the ocular surface.

STTR Subcontract (Flood/Egan) 8/1/09-7/31/10

TheraLogics (NIH R41 HL095293-01A2)
NF-kappa B Inhibition in Lung Ischemia-Reperfusion Injury

The major goal of this project is to determine if inhibition of NF-kappa B can ameliorate lung ischemia-reperfusion injury, a particular problem in organ transplantation.

1 R01 HL 092964-01A1 (Boucher) 1/1/10-12/31/13

NIH/NHLBI

The Role of Anaerobic Bacterial Infection in Cystic Fibrosis

The major goal of this project is to test the hypothesis that obligate anaerobic bacteria are pathogens in the CF lung and to identify when they produce this pathogenic effect.

Completed Research Support

RANDEL07P0 (Randell) 3/1/07-2/28/10

Cystic Fibrosis Foundation

Dysregulated Airway Physiology in Scnn1b Transgenic Mice

The major goal of this project is to elucidate key mechanisms by which defective mucus clearance results in chronic airway injury by: 1) studying the interaction between tethered and secreted mucins to examine mechanisms of mucus adhesion, plaque formation and airway obstruction, 2) determining causes and effects of airway inflammation and goblet cell metaplasia in Scnn1b mice, and 3) examining the pathogenesis of respiratory virus-induced airway disease in Scnn1b mice.

BOUCHE08P0 Boucher (PI) 7/1/08-6/30/09

Cystic Fibrosis Foundation

The Role of Anaerobic Bacterial Infection in Cystic Fibrosis

The major goal of this project is to test the hypothesis that obligate anaerobic bacteria are pathogens in the CF lung and to identify when they produce this pathogenic effect.

Role: Co-Investigator