#### **CURRICULUM VITAE**

## I. Personal Information (current as of November 2020)

Name: Lawrence S. (Lance) Prince, MD, PhD

**Professor of Pediatrics** 

Division Chief, Neonatal Developmental Medicine

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## II. Educational Background

9/1985-5/1989 B.S. Chemistry, University of Miami, Coral Gables, FL

6/1989-7/1996 M.D. University of Alabama School of Medicine, Birmingham, AL (Medical

Scientist Training Program)

6/1991-6/1995 Ph.D. Cell Biology, University of Alabama at Birmingham,

Birmingham, AL (Medical Scientist Training Program)

8/1996-6/1997,

7/1998-6/1999 Postdoctoral Fellow, Department of Internal Medicine, University of Iowa

(Michael J. Welsh, Mentor)

6/1997-6/1998,

7/1999-6/2000 Resident Physician, Pediatrics, University of Iowa (Special Alternative Pathway

for Pediatric Trainees)

7/2000-12/2002 Fellow in Neonatology, Pediatrics, University of Iowa

### III. Licensure and Certification

Medical Board of California, 2013-present, #G89291

Board Certified in: Pediatrics, 2003

Neonatal-Perinatal Medicine, 2005

## IV. Professional Appointments

1/2003-6/2007	Assistant Professor of Pediatrics, Division of Neonatology, University of Alabama at Birmingham
2003	Secondary Appointment, UAB Department of Cell Biology
2003	Secondary Appointment, UAB Department of Physiology and Biophysics
2003-2007	Associate Scientist, UAB Comprehensive Cancer Center.
2003-2007	Member, UAB Gregory Fleming James Cystic Fibrosis Research Center.
7/2007-9/2011	Assistant Professor of Pediatrics, Division of Neonatology, Vanderbilt University School of Medicine
9/2011-1/2013	Associate Professor of Pediatrics, Division of Neonatology, Vanderbilt University School of Medicine
11/2008-1/2013	Joint Appointment, Department of Cell and Developmental Biology, Vanderbilt University
7/2009-1/2013	Faculty Member, Vanderbilt Center for Stem Cell Biology
2/2013-12/2014	Adjunct Professor, Vanderbilt University School of Medicine
2/2013-6/2018	Associate Professor of Pediatrics, Division Chief of Neonatology, University of California, San Diego; Rady Children's Hospital, San Diego
7/2018-11/2020	Professor of Pediatrics, Division Chief of Neonatology, University of California, San Diego; Rady Children's Hospital, San Diego
11/2020-present	Professor of Pediatrics, Division Chief of Neonatal and Developmental Medicine, Stanford School of Medicine; Lucile Packard Children's Hospital

## V. Honors and Awards

- 1999 Fellow Basic Research Award, Society for Pediatric Research. "Keratinocyte Growth Factor Stimulation of Human Airway Epithelia: Microarray Analysis of Gene Expression Uncovers a Role in Interferon Signaling."
- 2000 Trainee Investigator Award, Midwest Society for Pediatric Research. "Exposure of Human Airway Epithelia to Air-Liquid Interface Changes the Redox State and Promotes Differentiation."
- National Staff Research Award, American Lung Association.

## **VI. Scholarly Publications**

### A. Peer-reviewed articles:

- 1. **Prince LS**, Miller SK, Pohost GM, Elgavish GA. The longitudinal relaxation time (T1) of the intracellular 23Na NMR signal in the isolated perfused rat heart during hypoxia and reoxygenation. *Magn Reson Med*. 1992; 23(2): 376-382.
- 2. **Prince LS**, Tousson A, Marchase RB. <u>Cell surface labeling of CFTR in T84 cells. *Am J Physiol*.</u> 1993; 264(2 Pt 1): C491-498.
- 3. **Prince LS**, Workman RB Jr, Marchase RB. <u>Rapid endocytosis of the cystic fibrosis</u> transmembrane conductance regulator chloride channel. *Proc Natl Acad Sci U S A*. 1994; 91(11): 5192-5196.
- 4. Snyder PM, Cheng C, **Prince LS**, Rogers JC, Welsh MJ. <u>Electrophysiological and biochemical evidence that DEG/ENaC cation channels are composed of nine subunits.</u> *J.Biol Chem.* 1998; 273(2): 681-684.
- 5. Cheng C, **Prince LS**, Snyder PM, Welsh MJ. <u>Assembly of the epithelial Na+ channel evaluated using sucrose gradient sedimentation analysis. *J Biol Chem.* 1998; 273(35): 22693-22700.</u>
- 6. Goulet CC, Volk KA, Adams CM, **Prince LS**, Stokes JB, Snyder PM. <u>Inhibition of the epithelial Na+ channel by interaction of Nedd4 with a PY motif deleted in Liddle's syndrome</u>. *J Biol Chem.* 1998; 273(45): 30012-30017.
- 7. **Prince LS**, Welsh MJ. <u>Cell surface expression and biosynthesis of epithelial Na+ channels</u>. *Biochem J.* 1998; 336 (Pt 3): 705-710.
- 8. **Prince LS**, Peter K, Hatton SR, Zaliauskiene L, Cotlin LF, Clancy JP, Marchase RB, Collawn JF. Efficient endocytosis of the cystic fibrosis transmembrane conductance regulator requires a tyrosine-based signal. *J Biol Chem.* 1999; 274(6): 3602-3609.
- 9. **Prince LS**, Welsh MJ. Effect of subunit composition and Liddle's syndrome mutations on biosynthesis of ENaC. *Am J Physiol: Cell Physiol*. 1999; 276: C1346-C1351.

- Prince LS, Launspach JL, Geller DS, Lifton RP, Pratt JH, Zabner J, Welsh MJ. <u>Absence of amiloride-sensitive sodium absorption in the airway of an infant with pseudohypoaldosteronism</u>. J Pediatr. 1999; 135(6): 786-789.
- 11. **Prince LS**, Karp PH, Moninger TO, Welsh MJ. <u>KGF alters gene expression in human airway epithelia: potential regulation of the inflammatory response. *Physiol Genomics* 2001; 6: 81-89.</u>
- 12. **Prince LS**, Okoh VO, Moninger TO, and Matalon S. Lipopolysaccharide Increases Alveolar Type II Cell Number in Fetal Mouse Lungs through Toll-Like Receptor 4 and NF-κB. *Am J Physiol: Lung Cell Mol Physiol* 2004; 287: L999-1006.
- 13. **Prince LS**, Dieperink HD, Okoh VO, Fierro-Perez GA, Lallone RL. Toll-like receptor signaling inhibits fetal mouse lung branching. *Dev Dyn* 2005; 233(2): 553-561.
- 14. Dieperink HD, Blackwell TS, **Prince LS**. <u>Hyperoxia and apoptosis in developing lung mesenchyme</u>. *Ped Res* 2006 Feb; 59(2): 185-190.
- 15. Benjamin JT, Smith RJ, Halloran BA, Day TJ, Kelly DR, **Prince LS**. <u>FGF-10 is decreased in bronchopulmonary dysplasia and suppressed by Toll-like receptor activation.</u> *Am J Physiol: Lung Cell Mol Physiol* 2007 Feb; 292(2): L550-558.
- 16. Wang H, Ding T, Brown N, Yamamoto Y, **Prince LS**, Reese J, Paria BC. Zonula occludens-1 (ZO-1) is involved in morula to blastocyst transformation in the mouse. *Dev Biol.* 2008 Jun 1; 318(1):112-125.
- 17. Benjamin JT, Gaston DC, Halloran BA, Schnapp LM, Zent R, **Prince LS**. The role of integrin α8β1 in fetal lung morphogenesis and injury. *Dev Biol*. 2009 Nov 15; 335(2): 407-417.
- 18. Miller JD, Benjamin JR, Kelly DR, Frank DB, **Prince LS**. Chorioamnionitis Stimulates Angiogenesis in Saccular Stage Fetal Lungs Via CC Chemokines. *Am J Physiol: Lung Cell Mol Physiol*. 2010 Feb 19; 298: L637-L645.
- Benjamin JT, Carver BJ, Plosa EJ, Yamamoto Y, Miller JD, Liu J-H, van der Meer R, Blackwell TS, Prince LS. NF-kappaB activation limits airway branching through inhibition of Sp1-mediated FGF-10 expression. *J Immunol*. 2010 Oct 15; 15(8): 4896-4903.
- 20. McElroy SJ, **Prince LS**, Weitkamp JH, Reese J, Slaughter JC, Polk DB. <u>Tumor Necrosis Factor Receptor 1-Dependent Depletion of Mucus in Immature Small Intestine: A Potential Role in Neonatal Necrotizing Enterocolitis</u>. *Am J Physiol Gastrointest Liver Physiol*. 2011 Oct 301(4): G656-66.

- 21. Blackwell TS, Hipps AN, Yamamoto Y, Han W, Barham WJ, Ostrowski MC, Yull FE, **Prince LS**. NF-κB Signaling in Fetal Lung Macrophages Disrupts Airway Morphogenesis. *J Immunol*. 2011 Sep 1; 187(5): 2740-7.
- 22. Zaynagetdinov R, Stathopoulos GT, Sherrill TP, Cheng DS, McLoed AG, Ausborn JA, Polosukhin VV, Connelly L, Zhou W, Fingleton B, Peebles RS, **Prince LS**, Yull FE, Blackwell TS. Epithelial nuclear factor-κB signaling promotes lung carcinogenesis via recruitment of regulatory T lymphocytes. *Oncogene*. 2012 Jun 28;31(26):3164-76.
- 23. Yamamoto Y, Baldwin HS, **Prince LS**. Endothelial Differentiation by Multipotent Fetal Mouse Lung Mesenchymal Cells. Stem Cells Dev. 2012 Jun 10;21(9):1455-65.
- 24. Humphreys R, Zheng W, **Prince LS**, Qu X, Brown C, Loomes K, Huppert SS, Baldwin S, Goudy S. <u>Cranial neural crest ablation of Jagged1 recapitulates the craniofacial phenotype of Alagille syndrome patients. *Hum Mol Genet*. 2012 Mar 15;21(6):1374-83</u>
- 25. Zhang C, Sherman MP, **Prince LS**, Bader D, Weitkamp JH, Slaughter JC, McElroy SJ. Paneth cell ablation in the presence of Klebsiella pneumoniae induces necrotizing enterocolitis (NEC)-like injury in immature murine small intestine. *Dis Model Mech*. 2012 Jul;5(4):522-32.
- 26. Fike CD, Sidoryk-Wegrzynowicz M, Aschner M, Summar M, **Prince LS**, Cunningham G, Kaplowitz M, Zhang Y, Aschner JL. <u>Prolonged hypoxia augments L-citrulline transport by System A in the newborn piglet pulmonary circulation</u>. *Cardiovasc Res*. 2012 Aug 1;95(3):375-84.
- 27. Plosa EJ, Gooding KA, Zent R, **Prince LS**. Non-muscle myosin II regulation of lung epithelial morphology. *Dev Dyn*. 2012 Nov;241(11):1770-81.
- 28. Goudy S, Angel P, Jacobs B, Hill C, Mainini V, Smith AL, Kousa YA, Caprioli R, **Prince LS<sub>2</sub>** Baldwin HS, Schutte BC. Cell-Autonomous and Non-Cell-Autonomous Roles for *Irf6* during Development of the Tongue. *PLoS ONE* 2013 Feb: 8(2): e56270.
- 29. Sen P, Yang Y, Navarro C, Silva I, Szafranski P, Kolodziejska KE, Dharmadhikari AV, Mostafa H, Kozakewich H, Kearney D, Cahill JB, Whitt M, Bilic M, Margraf L, Charles A, Goldblatt J, Gibson K, Lantz PE, Garvin AJ, Petty J, Kiblawi Z, Zuppan C, McConkie-Rosell A, McDonald MT, Peterson-Carmichael SL, Gaede JT, Shivanna B, Schady D, Friedlich PS, Hays SR, Palafoll IV, Siebers-Renelt U, Bohring A, Finn LS, Siebert JR, Galambos C, Nguyen L, Riley M, Chassaing N, Vigouroux A, Rocha G, Fernandes S, Brumbaugh J, Roberts K, Ho-Ming L, Lo IF, Lam S, Gerychova R, Jezova M, Valaskova I, Fellmann F, Afshar K, Giannoni E, Muhlethaler V, Liang J, Beckmann JS, Lioy J, Deshmukh H, Srinivasan L, Swarr DT, Sloman M, Shaw-Smith C, van Loon RL, Hagman C, Sznajer Y, Barrea C, Galant C, Detaille T, Wambach JA, Cole FS, Hamvas A, Prince LS, Diderich KE, Brooks AS, Verdijk RM, Ravindranathan H, Sugo E, Mowat D, Baker ML, Langston C, Welty S, Stankiewicz P. Novel FOXF1 mutations

- in sporadic and familial cases of alveolar capillary dysplasia with misaligned pulmonary veins imply a role for its DNA binding domain. *Hum Mutat.* 2013 Jun;34(6):801-11
- 30. Carver BJ, Plosa EJ, Stinnett AM, Blackwell TS, **Prince LS**. <u>Interactions between NF-κB and SP3 connect inflammatory signaling with reduced FGF-10 expression</u>. *J Biol Chem.* 2013 May 24;288(21):15318-25.
- 31. Greer RM, Miller JD, Okoh VO, Halloran BA, **Prince LS**. <u>Epithelial-mesenchymal coculture model for studying alveolar morphogenesis</u>. *Organogenesis*. 2014 May 14;10(3).
- 32. Stouch AN, Zaynagetdinov R, Barham WJ, Stinnett AM, Slaughter JC, Yull FE, Hoffman HM, Blackwell TS, **Prince LS**. IkB Kinase Activity Drives Fetal Lung Macrophage Maturation along a Non-M1/M2 Paradigm. *J Immunol*. 2014 Aug 1;193(3):1184-93. PMID: 24981452.
- 33. Plosa EJ, Young LR, Gulleman PM, Polosukhin VV, Zaynagetdinov R, Benjamin JT, Im AM, van der Meer R, Gleaves LA, Bulus N, Han W, **Prince LS**, Blackwell TS, Zent R. Epithelial Beta1 Integrin is Required for Lung Branching Morphogenesis and Alveolarization. *Development*. 2014 Dec;141(24):4751-62. PMID: 25395457.
- 34. Han W, Zaynagetdinov R, Yull FE, Polosukhin VV, Gleaves LA, Tanjore H, Young LR, Peterson TE, Manning HC, **Prince LS**, Blackwell TS. <u>Molecular Imaging of Folate Receptor Beta Positive Macrophages During Acute Lung Inflammation</u>. *Am J Respir Cell Mol Biol*. 2015 Jul;53(1):50-9. PMID: 25375039.
- 35. Stouch AN, McCoy AM, Greer RM, Lakhdari O, Yull FE, Blackwell TS, Hoffman HM, **Prince LS**. <u>IL-1β And Inflammasome Activity Link Inflammation To Abnormal Fetal Airway Development</u>. *J Immunol*. 2016 Apr 15;196(8):3411-20. PMID: 26951798.
- 36. Benjamin JT, van der Meer R, Im AM, Plosa EJ, Zaynagetdinov R, Burman A, Havrilla ME, Gleaves LA, Polosukhin VV, Deutsch GH, Yanagisawa H, Davidson JM, **Prince LS**, Young LR, Blackwell TS. <u>Epithelial-Derived Inflammation Disrupts Elastin Assembly and Alters Saccular Stage Lung Development.</u> *Am J Pathol.* 2016 Jul;186(7):1786-800. PMID: 27181406.
- 37. Lakhdari O, McAllister CS, Wang M, Minev I, **Prince LS**, Eckmann L, Kagnoff MF. <u>TLR3 signaling is downregulated by a MAVS isoform in epithelial cells.</u> *Cell Immunol*. 2016 Dec;310:205-210. PMID 27593154.
- 38. Medal RM, Im AM, Yamamoto Y, Lakhdari O, Blackwell TS, Hoffman HM, Sahoo D, **Prince LS**. The Innate Immune Response in Fetal Lung Mesenchymal Cells Targets <u>VEGFR2 Expression and Activity</u>. *Am J Physiol Lung Cell Mol Physiol*. 2017 Mar 23. PMID:28336813.
- 39. McCoy AM, Herington JL, Stouch AN, Mukherjee AB, Lakhdari O, Blackwell TS, **Prince LS**. <u>IKKβ Activation in the Fetal Lung Mesenchyme Alters Lung Vascular</u>

- <u>Development but Not Airway Morphogenesis</u>. *Am J Pathol*. 2017 Dec;187(12):2635-2644. PMID: 28923684.
- 40. Oppong-Nonterah GO, Lakhdari O, Yamamura A, Hoffman HM, **Prince LS**. <u>TLR</u> <u>Activation Alters Bone Marrow Derived Macrophage Differentiation</u>. *J Innate Immun*. 2018 Nov 8:1-10. PMID: 30408777.
- 41. Lakhdari O, Yamamura A, Hernandez GE, Anderson KK, Lund SJ, Oppong-Nonterah GO, Hoffman HM, **Prince LS**. <u>Differential Immune Activation in Fetal Macrophage Populations</u>. *Sci Rep*. 2019 May 22;9(1):7677. PMID: 31118442.
- 42. Kingsmore SF, Cakici JA, Clark MM, Gaughran M, Feddock M, Batalov S, Bainbridge MN, Carroll J, Caylor SA, Clarke C, Ding Y, Ellsworth K, Farnaes L, Hildreth A, Hobbs C, James K, Kint CI, Lenberg J, Nahas S, **Prince L**, Reyes I, Salz L, Sanford E, Schols P, Sweeney N, Tokita M, Veeraraghavan N, Watkins K, Wigby K, Wong T, Chowdhury S, Wright MS, Dimmock D. <u>A Randomized, Controlled Trial of the Analytic and Diagnostic Performance of Singleton and Trio, Rapid Genome and Exome Sequencing in Ill Infants. *Am J Hum Genet*. 2019 Oct 3;105(4):719-733. PMID: 31564432; PMCID: PMC6817534.</u>
- 43. Sajti E, Link VM, Ouyang Z, Spann NJ, Westin E, Romanoski CE, Fonseca GJ, **Prince** LS, Glass CK. <u>Transcriptomic and epigenetic mechanisms underlying myeloid diversity in the lung</u>. *Nat Immunol*. 2020 Feb;21(2):221-231. PMID: 31959980.
- 44. Dang D, Taheri S, Das S, Ghosh P, **Prince LS**, Sahoo D. <u>Computational Approach to Identifying Universal Macrophage Biomarkers</u>. *Front Physiol*. 2020 Apr 11:275. PMID: 32322218.
- 45. Sahoo D, Zaramela LS, Hernandez GE, Mai U, Taheri S, Dang D, Stouch AN, Medal RM, McCoy AM, Aschner JL, Blackwell TS, Zengler K, **Prince LS**. <u>Transcriptional Profiling of Lung Macrophages from Preterm Infants Identifies Disease Related Programs</u>. *Commun Biol*. 2020 May 22;3(1):259. PMID: 32444859.
- 46. Lund SJ, Patras KA, Kimmey JM, Yamamura A, Butcher LD, Del Rosario PGB, Hernandez GE, McCoy AM, Lakhdari O, Nizet V, **Prince LS**. <u>Developmental Immaturity of Siglec Receptor Expression on Neonatal Alveolar Macrophages Predisposes to Severe Group B Streptococcal Infection.</u> *iScience*. 2020 May 28;23(6):101207. PMID: 32535023

## **B.** Other Peer-Reviewed Publications:

Carlo WA, **Prince LS**, St. John EB, Amabalavanan N. <u>Care of very low birth weight infants with respiratory distress syndrome: an evidence-based review.</u> *Minerva Pediatr* 2004 Aug: 56(4): 373-80.

**Prince LS**. (2011) Growth Factors in Pulmonary Hypertension. Guilty Parties or Just Bystanders? *Advances in Pulmonary Hypertension*. Vol 9(3).

Morrisey EE, Cardoso WV, Lane RH, Rabinovitch M, Abman SH, Ai X, Albertine KH, Bland RD, Chapman HA, Checkley W, Epstein JA, Kintner CR, Kumar M, Minoo P, Mariani TJ, McDonald DM, Mukouyama YS, **Prince LS**, Reese J, Rossant J, Shi W, Sun X, Werb Z, Whitsett JA, Gail D, Blaisdell CJ, Lin QS. <u>Molecular determinants of lung development</u>. *Ann Am Thorac Soc.* 2013 Apr;10(2):S12-6.

**Prince LS.** FGF10 and Human Lung Disease Across the Life Spectrum. Front Genet. 2018 Oct 31;9:517.

## **C. Editorials:**

**Prince LS**. Hyperoxia and EGFL7: Saving cells from too much of a good thing. *Am J Physiol: Lung Cell Mol Physiol.* 2008 Jan; 294(1):L15-6.

### **D. Book Chapters:**

Davis IC, **Prince LS**, Matalon S. (2005) Epithelial Sodium Channel Function in Health and Disease in the Adult Lung. in Yuan JX-J (ed.) *Ion Channels in the Pulmonary Vasculature. Lung Biology in Health and Disease*, San Diego, CA: Marcel Dekker.

Jones PL and **Prince LS**. (2011) The Extracellular Matrix in Development (4<sup>th</sup> Edition). Polin RA, Fox WW, and Abman SH (ed.) *Fetal and Neonatal Physiology*, Philadelphia, PA: Elsevier Saunders.

#### VII. Grants

#### A. Current

1R01AI142864-01A1, National Institute of Allergy and Infectious Diseases "Glycan-Lectin Receptor Regulation of Macrophage Maturation and Lung Innate Defenses in the Fetus and Newborn Infant."

Muti-PI: Lawrence S. Prince

Multi-PI: Victor Nizet 07/17/2019-06/30/2022

This project brings together expertise in developmental immunology and host-pathogen interactions to investigate the molecular and cellular mechanisms leading to the unique susceptibility of newborns to pneumonia. Using both novel mouse models and mutant bacteria, experiments will examine host-pathogen interactions in newborn animals to understand at a basic level how specific bacteria cause neonatal lung disease. This project will also test the hypothesis that pathogenic bacteria use molecular mimicry to exploit a novel immune tolerance mechanism important for normal fetal development.

1R01HL143256-01, National Heart Lung and Blood Institute

"Impact of Early-in-life Disruption of Lung Development on Adult Lung Progenitor Function."

Multi-PI: Xin Sun

Multi-PI: Lawrence S. Prince

08/22/2018-06/30/2022

This project tests how early exposures to lung injury impact repair and regeneration processes in adult lungs. Experiments will measure the long-lasting effects of perinatal lung injury on cell differentiation, progenitor cell biology, and epigenetic imprinting throughout each lung cell population. Our findings will identify specific mechanisms that link early developmental factors to adult disease.

1U01HL148867, National Heart Lung and Blood Institute

"Decoding the Cellular Niches Critical for Lung Maturation and Pathogenesis"

PI: Xin Sun (Lawrence S. Prince, Co-Investigator)

08/19/19-06/30/24

The goal of this study is to use cutting-edge genomic, epigenomic and imaging technologies to systematically define the exciting kaleidoscope of cell types in the whole lung, with an emphasis on cellular niches that are central to pathogenesis. We expect that our findings generated under the organization of the LungMap will serve as a powerful community resource, and advance our knowledge of lung maturation and pediatric lung diseases.

1R01HL142215, National Heart Lung and Blood Institute

"Genetic Basis of Normal and Pathological Alveologenesis in Lung Development"

PI: Xin Sun (Lawrence S. Prince, Co-Investigator)

08/22/2018-06/30/2022

The goal of this study is to test the hypothesis that the proper control of the number, organization, as well as tensile property of alveolar myofibroblasts is essential for generating new gas-exchange surface area. Our findings will provide insights for more effective treatment of BPD as well as how to regenerate gas-exchange surfaces in premature lungs.

## **B.** Prior

1R01HL126703-01, National Heart Lung and Blood Institute

"Transcriptional Control of Lung Macrophage Development"

Multi-PI: Lawrence S. Prince

Multi-PI: Harold M. Hoffman

04/01/2015-03/31/2020

These experiments within this proposal will identify key basic mechanisms regulating how the lung innate immune system develops in both normal and disease settings. Our findings will therefore lay the foundation for future translational and therapeutic discovery and applications to improve pediatric health.

20180324. The Gerber Foundation

"Machine Learning Approaches for Discovering the Molecular Basis of Neonatal Lung Disease" PI: Lawrence S. Prince

01/01/18-12/31/19

This proposal uses a novel machine learning approach to identify patterns of gene expression that correlate with disease progression in preterm infants developing bronchopulmonary dysplasia. Over 200 gene expression profiles of lung macrophages obtained from intubated patients will be analyzed along with in depth clinical metadata to determine how macrophage transcription predicts clinical outcomes and how clinical events and risk factors influence lung immunity.

2R01HL086324-06A1, National Heart Lung and Blood Institute

"FGF-10 Expression in a Fetal Mouse Lung Model of Bronchopulmonary Dysplasia."

PI: Lawrence S. Prince

04/15/2008 - 05/31/2019

This grant examines the signaling mechanisms in the fetal mouse lung that connect inflammation to disruption of normal FGF-10 expression in the developing lung. Studies investigate how TLR signaling and inflammasome expression and function are regulated during fetal lung development. Molecular approaches are focused on how specific inflammatory mediators regulate transcriptional regulation of the FGF-10 promoter.

1823-3830, The Gerber Foundation

"Genomics of Lung Inflammation in Preterm Infants"

PI: Lawrence S. Prince

08/01/2014-07/31/2017

This proposal will use innovative genomic approaches to determine the gene expression profile of lung macrophages in preterm infants. These data will help identify which patients are most likely to develop chronic disease and may also uncover new targets for prevention and treatment of lung disorders in neonates.

2014 Pilot Project (CIIPLSP), UCSD Clinical & Translational Research Institute

"Personalized Genomic Medicine in Preterm Infants"

PI: Lawrence S. Prince 04/01/2014-03/31/2015

This pilot project will perform genomic analysis of macrophages isolated from the lungs of preterm infants. Bioinformatic approaches will correlate gene expression signatures with bronchopulmonary dysplasia incidence and disease severity. Using entirely human samples, these studies will develop personalized genomic approaches for preventing and treating neonatal lung disease.

1001328-AWD CR30 Prince, Rady Children's Hospital

"Personalized Genomic Medicine for Neonatal Lung Disease"

PI: Lawrence S. Prince

05/01/2014-04/30/2015

This patient-based genomic discovery study will measure and analyze the transcriptomic signatures in neonates with respiratory failure requiring mechanical ventilation. The goal of this cell-based and genome-wide approach is to identify discrete molecular signatures in individual patients that will predict disease severity and outcome

1R01HL097195, National Heart Lung and Blood Institute

"Role of Fetal Lung Macrophages in Bronchopulmonary Dysplasia."

PI: Lawrence S. Prince 07/01/2009-07/31/2015

This proposal tests the role of fetal lung macrophages in bronchopulmonary dysplasia pathogenesis. Specifically, we will test if macrophages are required for inhibition of normal lung development by innate immune stimuli, if NF-kappaB activation in macrophages mediates global fetal lung inflammation, and how early exposure of fetal lung macrophages to inflammatory stimuli alters macrophage phenotype as lungs mature.

### 1R01HL116358-01, National Heart Lung and Blood Institute

"Imaging Activated Macrophages in the Lungs."

Co-PI: Timothy Blackwell Co-PI: Lawrence S. Prince 09/01/2012-08/31/2015

This multiple PI grant will develop novel strategies for imaging activated lung macrophages in vivo.

## 1U01HL101456-01, National Heart Lung and Blood Institute

"Improving Prematurity-Related Respiratory Outcomes at Vanderbilt (IMPROV)."

PI: Judy L. Aschner (Lawrence S. Prince, Co-Investigator)

5/1/2010-4/30/2015

This grant is part of a multi-center program (Pulmonary and Respiratory Outcomes of Prematurity-PROP) that will better define the phenotypes and mechanisms in preterm infants that lead to chronic pulmonary disease.

### 3R01HL086324-02S1, National Heart Lung and Blood Institute

Supplement to "FGF-10 Expression in a Fetal Mouse Lung Model of Bronchopulmonary Dysplasia."

PI: Lawrence S. Prince 07/01/2009-06/30/2011

This supplemental grant supports research studying how inflammatory signals regulate FGF-10 transcription by novel mechanisms.

#### 1S10RR027396, National Center for Research Resources

"Confocal Microscope for Live Embryo Imaging in a Shared Resource Facility."

PI: Lawrence S. Prince 7/31/2010-8/1/2011

This grant supports the purchase of a live embryo/live tissue laser scanning confocal microscope to be shared among a group of developmental biologists studying the molecular mechanisms of 3-dimensional tissue morphogenesis.

## 5-FY07-555, March of Dimes

Basil O'Connor Starter Scholar Award

"Mechanisms of Altered Lung Morphogenesis in Bronchopulmonary Dysplasia."

PI: Lawrence S. Prince

7/1/2007-6/30/2009

This grant investigated how airway elongation and branching may be altered in experimental models of bronchopulmonary dysplasia.

Advancing Newborn Medicine Fellowship Grant, INO Therapeutics

"Inflammation Alters Fetal Lung Development by Decreasing Alpha-8 Intergrin Expression."

Trainee: John T. Benjamin Mentor: Lawrence S. Prince

2006-2007

This project examined the role of alpha8 integrin on fetal mouse lung morphogenesis.

Advancing Newborn Medicine Fellowship Grant, INO Therapeutics

"Mechanisms Regulating Mesenchymal Cell Migration During Alveolarization."

Trainee: J. Davin Miller Mentor: Lawrence S. Prince

2006-2007

This grant supported the development of a novel experimental model of alveolarization.

Neonatal Fellowship Grant, Discovery Laboratories

"Role of Toll-Like Receptor Signaling in Distal Airway Elongation."

Trainee: J. Davin Miller Mentor: Lawrence S. Prince

1/1/2006-12/31/2006

This project measured the effects of bacterial products and Toll Receptor agonists on mouse saccular airway elongation.

RG-10721-N, American Lung Association

Biomedical Research Grant

"Toll-Like Receptor Signaling and Cell-Matrix Interactions in the Fetal Lung Mesenchyme."

PI: Lawrence S. Prince

7/1/2005-6/30/2007

This project investigated myofibroblast differentiation in the fetal mouse lung and the effects of innate immune signaling on mesenchymal cell migration and adhesion to extracellular matrix.

U10 HD 34216-11, National Institute for Child Health and Human Development

"Multicenter Network of Neonatal Intensive Care Units"

Waldemar A. Carlo (Principal Investigator)

Lawrence Prince (Co-Investigator)

4/1/2006-3/31/2011

The major goals of this project are to work with the NICHD and the Steering Committee to prioritize, plan, implement, analyze, interpret, and report a series of randomized and observational studies.

NICHD43397, National Institute for Child Health and Human Development

Child Health Research Center Grant

"Modulation of Sodium and Fluid Transport in Fetal Lungs."

PI: Sergio Stagno (Lawrence S. Prince, Project PI)

7/01/2003-6/30/2006

This project studied the mechanisms by which bacterial endotoxin and inflammation alter epithelial sodium and water transport in fetal mouse lungs.

Research Institute Grant, Children's Hospital Foundation

"The Role of NF-kappaB and Toll Like Receptor 4 in Fetal Lung Development."

PI: Lawrence S. Prince

1/1/2003-12/31/2004

The major goal of this project was to determine the requirement of TLR4 signaling in fetal mouse lung development.

Parker B. Francis Foundation

Research Fellowship

"Gene Discovery and Expression Analysis in the Developing Mouse Lung"

Fellow: Lawrence S. Prince

Mentor: Bento Soares 7/1/2001-6/30/2004

The goal of this project was to isolate a subtracted, normalized cDNA library from fetal mouse lung, sequence and identify unique genes, and use these genes to perform genomic studies by custom microarray analysis.

### **Grants Completed During Training**

2002-2003	Children's Miracle Network (1392) "Microscopic Analysis of Abnormal Mouse Lung Development in Chorioamnionitis."
2001-2002	Advancing Newborn Medicine Fellowship Grant (Forrest Pharmaceuticals, Inc.) "Identification of Genes Under the Control of Corticotropin Releasing Hormone in the Developing Mouse Lung."
1998-2001	Individual National Research Service Award (F32 HL09831-01) NHLBI "Molecular Mechanisms of Liddle's Syndrome."
1996-1999	Cystic Fibrosis Foundation Fellowship (PRINCE96FO) "Effects of Liddle's Syndrome Mutations on Trafficking of ENaC."
1996-1997	Institutional Research Fellowship (Iowa Cardiovascular Center T32) "Molecular Mechanisms of Liddle's Syndrome."
1992-1995	Cystic Fibrosis Foundation Graduate Student Traineeship "Targeting of CFTR to the endocytic pathway"
1991-1992	March of Dimes Predoctoral Fellowship. "Cell-surface and Endosomal Targeting of CFTR."

#### **VIII. Clinical Trials**

### A. Current Trials

<u>Personalized Genomic Medicine in Preterm Infants/Genomics of Lung Inflammation in Preterm Infants.</u>

Project # 140240

March 2014-current

(Closed for enrollment after meeting target goals. Currently open for data analysis.)

## Role of Fetal Lung Macrophages in Bronchopulmonary Dysplasia.

Project #130315

May 2013-current

(Closed for enrollment after meeting target goals. Currently open for data analysis.)

#### X. Editorial Service

#### A. Editorial Board

American Journal of Physiology, Lung Cellular and Molecular Physiology.

## **B.** Reviewer

American Journal of Physiology

American Journal of Respiratory Cell and Molecular Biology

American Journal of Respiratory and Critical Care Medicine

BMC Biology

Clinical Science

Cvtokine

Development

**Developmental Dynamics** 

Experimental Lung Research

Expert Opinion on Pharmacotherapy

Expert Opinion on Therapeutic Targets

FASEB Journal

Frontiers in Genetics

Genome Research

Human Molecular Genetics

Journal of Applied Physiology

Journal of Immunology

Journal of Pathology

Journal of Pharmacy and Pharmacology

*JoVE* 

Molecular Biology of the Cell

Nature Communications

Neonatology

**Pediatrics** 

Pediatric Pulmonology Pediatric Research PLoS One Stem Cells Transgenic Research

## **XI. Service as Grant Reviewer**

## National Organizations

2009-2014	March of Dimes, Basil O'Connor Awards Review Committee
2009-2012	American Heart Association, Peer Review Committee: Lung, Respiration, and Resuscitation
2009, 2010	NIH, ad hoc reviewer, Study Section ZRG1 CB-N, S10 Applications on Confocal Microscopy and Cell Imaging Systems
2010	NIH, Review Group Member, NHLBI Special Review Group for RFA HL-10-026, "Programs of Excellence in Glycosciences (P01)"
2011-2019	NIH, ad hoc reviewer, Study Section LIRR (Lung Injury, Repair, and Remodeling).
2012	NIH, Review Group Member, Small Business Respiratory Sciences SEP (SBIR/STTR).
2013	NIH, Review Group Member, Endocrinology and Reproduction SEP (ZRG1 EMR-Q).
2013	NIH, Review Group Member, Stem Cell SEP (ZOD1 CM-6).
2015	NIH, Review Group Member, Lung Diseases SEP (ZRG1 CVRS-G).
2015	NIH, Review Group Member, Primary Prevention of Lung Disease SEP (ZHL1 CSR-H).
2016	NIH, Review Group Member, Prematurity-Related Ventilatory Control (PRE-VENT) SEP (ZHL1 CSR-H(M1)).
2016	NIH, Review Group Member, Limited Competition: Small Grant Program for NHLBI K01/K08/K23 Recipients (R03).
2017	NIH, Review Group Member, NHLBI SEP/SRG 2018/01 HLBP 1.
2018	NIH, Review Group Member, NHLBI Clinical Trials SEP/SRG 2018/05 (ZHL1 CSR-H (M1) 2).
2018	NIH, Review Group Member, NHLBI Clinical Trials SEP/SRG 2019/01 (ZHL1 CSR-H (F2) 2).

2019	NIH, Review Group Member, NHLBI Clinical Trials SEP/SRG 2019/05 (ZHL1 CSR-H (O1) 2).
2020	NIH, Chair, Scientific Review Group, Understanding the Early Development of the Immune System. ZRG1 EMNR-C(55) 2020/05.
2020	NIH, Review Group Member, NHLBI SEP/SRG 2020/03 (ZRG1 CVRS G (03)).

## International Organizations

- 2010-2011 <u>Italian Ministry of Health, International Reviewer for Clinical-Healthcare and Biomedical Research Projects.</u>
- Wellbeing of Women (UK), Reviewer for Research Project Grants.

## XII. University Administrative Service

## UCSD and Rady Children's Hospital Activities

2013-	Neonatology Steering Committee
2013-2017	UCSD Medical Staff Executive Committee
2013-	Women's and Infant's Services Executive Council
2013-2017	UCSD Medical Center Critical Care Committee
2013-2014	Medical Director, Infant Special Care Center, UCSD Medical Center
2013-	Medical Director, Neonatal Respiratory Therapy, UCSD Medical Center
2013-2015	Jacobs Medical Center NICU Planning Committee
2013	Children's Specialists of San Diego Board of Directors
2013-2016	UCSD Medical Center Pharmacy and Therapeutics Committee
2014	UCSD Radiology Chair Search Committee
2014	UCSD Health System Faculty Leadership Group
2014-	Children's Specialists of San Diego Revenue Cycle Committee
2014	UCSD NICU Strategy Group
2014	UCSD NICU QI Task Force

2014-	Children's Specialists of San Diego Compliance Committee
2016	Chair, Pediatric Critical Care Search Committee
2016-	Chair, Division of Neonatology Research Committee
2017-	Department of Pediatrics Bridge Funding Committee
2017	Division Chief of Pediatric Neurology Search Committee member
2017	Department of Pediatrics Physician Scientist Development Task Force
2018	Division Chief of Respiratory Medicine Search Committee member
2019-	Department of Pediatrics Research Symposium Planning Committee
2019	Department of Pediatrics Research Council
2019	Chair, Pediatric GI Division Chief Search Committee

## **XIII. Service to Professional Organizations**

## A. Membership

1997	American Academy of Pediatrics (Perinatal Section since 2004)
2005	American Society for Cell Biology
2005	American Physiological Society
2007	Society for Pediatric Research
2008	Perinatal Research Society
2011	American Association of Immunologists
2014	Western Society for Pediatric Research

## **B.** Committee Service

2006	Symposium Moderator, "Lung Development and Alveolarization." Society for Pediatric Research Annual Meeting, San Francisco, CA
2007	Symposium Moderator, "Lung Development and More." Society for Pediatric Research Annual Meeting, Toronto, Ontario

2009	Workshop Organizer, "Live Cell Imaging Approaches to Cell and Developmental Biology." Society for Pediatric Research Annual Meeting, Baltimore, MD
2009	Symposium Moderator, "Oxidant Signaling and Injury." Society for Pediatric Research Annual Meeting, Baltimore, MD
2010-2012	Society for Pediatric Research, Fellow Basic and Clinical Award Selection Committee
2013	<u>Platform Symposium Moderator</u> , "Fetal Origins of Adult Disease." Society for Pediatric Research Annual Meeting, Washington, DC

## C. Leadership Roles

2016-2019 <u>Council Member</u>, Western Society for Pediatric Research.

#### **XIV. Presentations**

- 2006 Invited Visiting Professor. Vanderbilt University School of Medicine, September 25, 2006. "Toll-Like Receptor Activation, Inflammation, and Abnormal Fetal Lung Development."
- 2006 Invited Seminar Speaker. Baylor University School of Medicine, Texas Children's Hospital, November 9, 2006. "Toll-Like Receptor Activation Inhibits Fetal Lung Development."
- 2008 Selected Poster Presentation, Gordon Conference. Fibroblast Growth Factors in Development and Disease, March 2-7. Lucca, Italy
- 2008 Invited Visiting Professor. University of Iowa College of Medicine, Division of Neonatal-Perinatal Medicine, April 2-4. "Bronchopulmonary Dysplasia: Searching for a Molecular Needle in a Chronic Disease Haystack;" "Toll-Like Receptor Activation and Abnormal Fetal Lung Development;" and "Early Career Development: Tales from the Trenches."
- 2009 Invited Speaker, Neonatology Research Conference. Children's Hospital of Philadelphia, February 26. "How does inflammation inhibit lung development in bronchopulmonary dysplasia?"
- 2009 Invited Platform Speaker. Southeastern Society for Developmental Biology. March 28. "The Role of Integrin α8β1-Fibronectin Interactions in Fetal Lung Morphogenesis."
- 2010 Invited Speaker, International Pulmonary Hypertension Conference. June 25. "Growth Factors in Pulmonary Hypertension. Guilty Parties or Just Bystanders?"
- 2011 Invited Speaker, Neonatal Grand Rounds. Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus, OH, January 21. "Inflammation and Arrested Lung Development in Bronchopulmonary Dysplasia."

- 2011 Invited Speaker, The Center for Developmental Lung Biology, Emory University School of Medicine, Atlanta, GA, March 18. "Macrophage Activation and Abnormal Fetal Lung Development. Potential Role in BPD."
- Visiting Consultant, University of Wisconsin School of Medicine, Madison, WI, April 14. Research Conference, "Inflammatory Regulation of FGF-10 Expression in the Developing Lung." Pediatric Grand Rounds, "Role of Inflammation in BPD Pathogenesis."
- 2011 Invited Speaker, Program in Developmental Biology and Neonatal Medicine, Riley Children's Hospital, Indiana University School of Medicine, Indianapolis, IN, April 26. "Mechanisms Linking Inflammation and Arrested Lung Development in Bronchopulmonary Dysplasia."
- 2011 Visiting Professor, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, May 6. "Molecular Mechanisms Linking Inflammation and Altered Lung Morphogenesis in Bronchopulmonary Dysplasia."
- 2011 Invited Speaker, Department of Pediatrics, University of Iowa Carver College of Medicine, Iowa City, IA, May 23. "Molecular Mechanisms Linking Inflammation and Arrested Lung Development in Bronchopulmonary Dysplasia."
- 2011 Invited Speaker, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, May 31. "Mechanisms Linking Inflammation and Altered Lung Development."
- 2011 Invited Speaker, Grand Rounds, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, September 13, "Mechanisms Linking Innate Immunity, Arrested Development, and Bronchopulmonary Dysplasia."
- 2012 Invited Speaker, Department of Pediatrics, University of California, San Diego, La Jolla, CA, May 7, "Inflammation, Altered Lung Development, and the Origins of Bronchopulmonary Dysplasia."
- 2013 Invited Presentation, PAS Topic Symposium, Chorioamnionitis and the Fetal Response to Inflammation: Effect on the Developing Fetus and on the Infant. "Intrauterine Infection and Lung Development.
- 2013 Invited Presentation, PAS Topic Symposium, Dysregulated Inflammation in the Preterm Infant A Common Pathway for Disease Risk and Long-Term Neurodevelopmental Impairment. "Development of Regulation of Inflammation in the Preterm Lung-Implications for Bronchopulmonary Dysplasia."
- 2014 State of the Art Lecture, Western Society for Pediatric Research, Carmel, CA, January 23. "Linking Inflammation and Abnormal Lung Development".

- 2014 Invited Speaker, The David Geffen School of Medicine at UCLA. Coronado Island, Coronado, CA March 1-3. "Inflammation and Altered Lung Development: A Lesson in Unintended Consequences."
- Visiting Professor, Yale University School of Medicine. New Haven, CT November 24. "Mechanisms Linking Inflammation and Abnormal Lung Development."
- 2015 Visiting Professor and Grand Rounds Speaker, UCLA Department of Pediatrics. Los Angeles, CA May 7-8. "Unintended Consequences: Why Fighting Infection is Bad for the Premature Lung."
- 2016 Visiting Professor, University of Colorado, Colorado Children's Hospital. Denver, CO March 8-10. "A Lesson in Collateral Damage: Lung Inflammation and Bronchopulmonary Dysplasia," and "Molecular Mechanisms Linking Inflammatory Signals and Abnormal Lung Development."
- 2016 Visiting Professor, Division of Pulmonary, Critical Care & Sleep Medicine University of Southern California, Los Angeles, CA. April 1. "Lung Development in Hostile Environments."
- 2016 Visiting Professor and Grand Rounds Speaker, Children's Hospital of Los Angeles, Los Angeles, CA. June 15-16. ""Why does fighting infection lead to abnormal lung development in preterm infants."
- 2017 State of the Art Lecturer, Advances in Neonatology and Pediatrics Conference, National Neonatology Forum India, Hyderabad, India. March 4-5. "The Ontogeny of the Neonatal Pulmonary Immune System" and "Bronchopulmonary Dysplasia: Can We Prevent It?"
- 2017 Invited Speaker, Gordon Conference on Lung Development, Injury, and Repair. New London, NH. August 20-25. "The Inflammasome and Developmental Regulation of Lung Inflammation"
- 2018 Invited Faculty, American Academy of Pediatrics Perinatal and Developmental Medicine Symposium. Snowmass, CO. June 6-9. "Formation of the Alveolar-Capillary Unit: The Developmental Biology Behind Limits of Viability" and "Is Bronchopulmonary Dysplasia a Vascular Disease?"
- 2018 Invited Speaker, FASEB Conference on the Lung Epithelium in Health and Disease. Olean, NY. July 29-August 3. "Role of Perinatal Inflammation in Bronchopulmonary Dysplasia."
- 2019 Guest Faculty, Sixth Annual Neonatal Cardiopulmonary Biology Young Investigators Forum. Chicago, IL. September 19-22. "Connecting the Dots between Inflammation and Abnormal Lung Development."

# **XV. Community Service**

2014-2019	Board of Directors, March of Dimes – San Diego and Imperial County Division ( <i>Board President 2015-2019</i> )
2016	Chair, San Diego and Oceanside March for Babies, March of Dimes
2015	External Reviewer, CHLA/USC Division of Neonatology
2015	External Reviewer, UCLA Division of Neonatology Fellowship Program
Advisory Activities	
2004-2008	Advisory Board, Discovery Laboratories (USA)
2017-2019	Advisory Board, Thrive Feeding, LLC (USA)