BIOGRAPHICAL SKETCH

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NAME: Aschner, Judy Lynn

eRA COMMONS USER NAME (credential, e.g., agency login): aschnejl

POSITION TITLE: Director, Member Scientist, Center for Discovery and Innovation, Hackensack Meridian *Health*; Professor of Pediatrics, Hackensack Meridian 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
Union College, Schenectady, NY	B.S.	06/1977	Biology
Univ of Rochester School of Medicine, Rochester, NY	M.D.	05/1981	Medicine
Univ of Rochester School of Medicine, Rochester, NY	Resident	06/1985	Pediatric Residency
Univ of Rochester School of Medicine, Rochester, NY	Fellowship	06/1988	Neonatology Fellowship
Albany Medical College, Albany, NY		06/1992	Parker B. Francis Research Fellowship

A. A. Personal Statement

I am a physician-scientist with long-standing NIH funding for my laboratory-based and clinical/translational research programs. My research bridges bench to bedside investigations, from mechanistic studies of altered signaling in the neonatal pulmonary circulation in animal models to large multi-center studies involving recruitment and long-term follow up of preterm and term cohorts. Funded by the NIH since 1998, I have served as PI on grants from NHLBI, NIEHS, NICHD and the Office of the Director. During my career I have focused on two major research areas: (a) novel therapies to prevent and treat neonatal lung diseases and (b) understanding and mitigating the impact of early life environmental exposures on long-term health outcomes for infants and children.

I have more than a decade of experience leading multi-site longitudinal human subjects research studies, working collaboratively with the NIH and PIs across the US. As PI at Vanderbilt for the Prematurity and Respiratory Outcomes Program (PROP; U01HL101456), I investigated molecular and genetic biomarkers in preterm infants at risk for bronchopulmonary dysplasia and long-term respiratory morbidity. I am currently NIH contact PI of a new multi-site pregnancy cohort (UG3OD035546, “Enriching ECHO with High-Risk Pregnancies and Children with Disabilities”), which is part of the national Environmental Influences on Child Health Outcomes (ECHO) program, and MPI of a continuing pediatric preterm cohort in ECHO, “Developmental Impact of NICU Exposures” (DINE; UG3OD035513) which has been funded since 2016. The goal of ECHO is to better understand the effects of physical, chemical, and biological exposures, social and behavioral factors, and the natural and built environments on child health and development. ECHO cycle 2 is funded until 2030.

Ongoing and recently completed projects that I would like to highlight include:

Funding Agency: NIH Office of the Director: Environmental Influences on Child Health Outcomes (ECHO) UG3OD035546; *Enriching ECHO Cohorts with High-risk Pregnancies and Children with Disabilities*
Dates: 09/01/2023-05/31/2025 Aschner JL: Principal Investigator; contact PI

Funding Agency: NIH Office of the Director: Environmental Influences on Child Health Outcomes (ECHO) UG3OD035513-01) *Developmental Impact of NICU Exposures (DINE)2*
Dates: 09/01/2023-05/31/2025 Stroustrup A, MPI, contact PI; Aschner JL MPI

Funding Agency: NIH
Post Acute Sequelae of Covid-19 (PASC) Investigators Consortium Phase 2: Researching COVID to Enhance Recovery (RECOVER) Katz, NYU PI; Kleinman L, Rutger’s PI, Aschner HMH site PI

Funding Agency: Burke Foundation, and Turrell Fund
Improving Health and Resiliency of At-risk NJ Families: HealthySteps 0-3 Pilot Project at Hackensack Meridian Health
Dates: 07/01/2020-06/31/2024 Aschner JL, PI

NIH R34 HL142995 Fike, C. PI; Aschner JL co-I
08/01/2018-07/31/2022
Pharmacokinetics and safety of oral L-citrulline in infants with bronchopulmonary dysplasia

B. Positions, Scientific Appointments, and Honors

Positions and Employment

12/23- present	Director, Member Scientist, HMH Center for Discovery and Innovation
11/18-2023	Marvin I. Gottlieb, M.D., Ph.D. Chair of Pediatrics, HUMC, Hackensack, NJ
11/18-2023	Physician-in-Chief, Joseph M. Sanzari Children's Hospital at HUMC, Hackensack, NJ
11/18-2023	Physician-in-Chief, Hackensack Meridian Children's Health, NJ
4/13-Present	Professor (with tenure) Albert Einstein College of Medicine, Bronx, NY
4/13-Present	Adjunct Professor, Vanderbilt University School of Medicine, Nashville, TN
4/13-2018	Michael I. Cohen M.D. University Chair of Pediatrics, Albert Einstein Coll of Med, Bronx, NY
4/13-2018	Physician-in-Chief, Children's Hospital at Montefiore, Bronx, NY
2008-3/13	Julia Carell Stadler Professor (with Tenure), Vanderbilt Univ Medical Center, Nashville, TN
7/04-3/13	Professor of Pediatrics, Vanderbilt University Medical Center, Nashville, TN Director of Neonatology, The Monroe Carell Jr. Children's Hospital at Vanderbilt
7/03-6/04	Professor of Pediatrics, Wake Forest University Health Sciences**,** Winston-Salem, NC
9/94-6/03	Associate Professor of Pediatrics, Wake Forest Univ. Health Sciences**,** Winston-Salem, NC
1994	Associate Professor of Pediatrics, Albany Medical College, Albany, NY
1988-1994	Assistant Professor of Pediatrics, Albany Medical College, Albany, NY
1988	Instructor in Pediatrics, Albany Medical College, Albany, NY

Other Experience and Professional Memberships

2018-present	National Board of Trustees: March of Dimes
2018-present	NHLBI Board of External Experts (BEE)
2018-2022	Chair: Federation of Pediatric Organizations (FOPO)
2013-present	International Perinatal Collegium
2012-2013	Hedwig van Ameringen Executive Leadership in Academic Medicine Program for Women
2012-2013	Chair: NIH BPD Primary Prevention Subcommittee
2012-2016	NHLBI Institutional Training Mechanism Review Committee
2011, 2012	NIH Pediatric Panel for Surgical Sciences, Biomedical Imaging & Bioengineering IRG (SBIB-V)
2011-2007	NIH Special Emphasis Panel/Ancillary Studies in Clinical Trials RFA
2010-2013	Vanderbilt Faculty Senate (elected Vice Chair 2011)
2009-present	Elected Member, Perinatal Research Society
2009-2014	Secretary-Treasurer: American Pediatric Society
2009-2014	Federation of Pediatric Organizations (FOPO) *Board of Directors*
2008-2014	Pediatric Academic Societies (PAS) Program Committee and Operating Committee
2007-2012	Am Board of Pediatrics, Neonatal-Perinatal Medicine Subboard and Credentialing Committee
2007-present	Member: American Pediatric Society
2007-2012	Strategic Planning Committee, AAP Section on Perinatal Pediatrics (Chair Leadership Domain)
2007-2005	NIH Special Emphasis Panel/Scientific Review Group 2005/10 ZRG1 RES-B (03)
2006-2009	NHLBI CLinical TRials Review Committee (CLTR)
2003-2007	Chair: Organization of Neonatology Training Program Directors (ONTPD) of the AAP
2002-present	Vice-Chairperson and member of the Executive Board of IPOKRaTES International
1999-2004	ACGME Standing Panel for Accreditation Appeals in Neonatal-Perinatal Medicine
1999-present	Member, Society for Pediatric Research
1989-present	Member, American Thoracic Society
1994-present	Member, AAP Section on Perinatal Pediatrics
1985-present	Fellow, American Academy of Pediatrics (AAP)

Honors

Peter Auld Invited Lecturer and visiting professor, Weill Cornell Medicine, NYC, NY (2024)
Diana Woo memorial lecture, University of Chicago, Chicago IL, (2024)
Babson Lecture, Doernbecher Children's Hospital, OHSU, Portland, OR (2018)
Jerry Elliot Memorial Lecture, AAP 42nd Southeastern Conference on Perinatal Research (2018)
Eastern Society for Pediatric Research Mentor of the Year Award (2017)
Elected to the Practitioners Society of New York (2015-present)
White Coat Ceremony Keynote Address "On Becoming a Physician": Albert Einstein Coll of Medicine (2015)
Samuel Clausen Lecturer: University of Rochester School of Medicine (2015)
The Gerald Merenstein Lecturer, AAP Section on Perinatal Pediatrics Keynote Address (2014)
The Alexander Award Lecture, NICHD Young Investigator's Workshop, Chicago, IL (2014)
The Joan Hodgman Lecture: Western Society for Pediatric Research (2014)
NICHD Lecturer: Perinatal Research Society Annual Meeting, Park City Utah (2012)
Robert Usher Visiting Professor: McGill University (2011)
Norman Kretchmer Visiting Professorship: Stanford University (2011)
The Wandra L. Jones-Phillips Memorial Lectureship: Emory University (2009)
The Reba Michels Hill Memorial Lectureship: Texas Children's Hospital (2008)

C. Contributions to Science

C.1 Neonatal Pulmonary Hypertension

Persistent pulmonary hypertension of the newborn (PPHN) is a life-threatening condition caused by the failure to achieve or sustain the normal decrease in pulmonary vascular resistance at birth. PPHN is a common condition among infants requiring neonatal intensive care that carries a 10-20% mortality. My early research career focused on basic research to improve understanding of the signaling mechanisms that regulate the neonatal pulmonary circulation and the factors that contribute to alterations in pulmonary vascular responses and PPHN. Funded by NHLBI [R01 HL62489 (04/01/99-03/31/04) and R01 HL075511 (04/01/05-03/31/10)], my laboratory investigated the role of the chaperone protein, Hsp90, and its client protein interactions in the regulation of vascular responses in the normal newborn pulmonary circulation, and during chronic hypoxia. In a series of publications, we demonstrated that Hsp90 binding to endothelial nitric oxide (eNOS) and other client proteins, including P23, regulates vascular tone and reactivity in the newborn pulmonary microcirculation. We also showed that chronic hypoxia disrupts Hsp90/client protein interactions bioavailability of the NO.

a. **Aschner JL**, Foster SL, Kaplowitz M, Zhang Y, Zeng H, Fike CD. Heat shock protein 90 modulates endothelial nitric oxide synthase activity and vascular reactivity in the newborn piglet pulmonary circulation. *Am J Physiol Lung Cell Mol Physiol.* 2007 Jun;292(6):L1515-1525. PMID: 17337508
b. **Aschner JL**, Zeng H, Kaplowitz MR, Zhang Y, Slaughter JC, Fike CD. Heat shock protein 90-eNOS interactions mature with postnatal age in the pulmonary circulation of the piglet. *Am J Physiol Lung Cell Mol Physiol.* 2009 Mar;296(3):L555-564. PMCID: PMC2660212
c. Fike CD, Pfister SL, Slaughter JC, Kaplowitz MR, Zhang Y, Zeng H, Frye NR, **Aschner JL**. Protein complex formation with heat shock protein 90 in chronic hypoxia-induced pulmonary hypertension in newborn piglets. *Am J Physiol Heart Circ Physiol.* 2010 Oct;299(4):H1190-1204. PMCID: PMC2957352
d. Dikalova AE, **Aschner JL**, Kaplowitz MR, Summar M, Fike CD. Tetrahydrobiopterin oral therapy recouples eNOS and ameliorates chronic hypoxia-induced pulmonary hypertension in newborn pigs. Am J Physiol Lung Cell Mol Physiol. 2016 Oct 1;311(4):L743-L753; Aug 19: doi: 10.1152/ajplung.00238.2016. PMID: 27542807; PMCID:PMC5142125

This early work led to the identification of the novel Hsp90 client proteins, argininosuccinate lyase (ASL) and argininosuccinate synthase (ASS), two enzymes in the urea cycle. L-citrulline, produced via the urea cycle is converted to L-arginine by ASS and ASL. In a series of publications, we showed that ASS and ASL are expressed in the lung, and form a complex with eNOS and other Hsp90 client proteins for the conversion of L-citrulline to L-arginine and delivery of arginine to eNOS for efficient production of NO. We further showed that deficiency of ASL (in a hypomorphic mouse model and in human ASL deficiency) leads to reduced NO production, NOS uncoupling, altered NO-dependent vascular responses, free radical excess and hypertension. We also identified the role of the neutral amino acid transporter, SNAT1, in modulating L-citrulline transport and NO signaling in piglet pulmonary arterial endothelial cells.

a. Erez A, Nagamani SC, Shchelochkov OA, Premkumar MH, Campeau PM, Chen Y, Garg HK, Li L, Mian A, Bertin TK, Black JO, Zeng H, Tang Y, Reddy AK, Summar M, O'Brien WE, Harrison DG, Mitch WE, Marini

JC, **Aschner JL**, Bryan NS, Lee B. Requirement of argininosuccinate lyase for systemic nitric oxide production. *Nat Med.* 2011 Nov 13;17(12):1619-1626. PMCID: PMC3348956

b. Fike CD, Sidoryk-Wegrzynowicz M, Aschner M, Summar M, Prince LS, Cunningham G, Kaplowitz M, Zhang Y, **Aschner JL**. Prolonged hypoxia augments L-citrulline transport by system A in the newborn piglet pulmonary circulation. *Cardiovasc Res.* 2012 Aug 01;95(3):375-384. PMCID: PMC3400357

c. Dikalova A, Fagiana A, **Aschner JL**, Aschner M, Summar M, Fike CD. Sodium-coupled neutral amino acid transporter 1 (SNAT1) modulates L-citrulline transport and nitric oxide (NO) signaling in piglet pulmonary arterial endothelial cells. *PLoS One.* 2014;9(1):e85730. PMCID: PMC3893279

d. Dikalova AE, **Aschner JL**, Zhang Y, Kaplowitz MR, Fike CD. Reactive oxygen species modulate sodium-coupled neutral amino acid transporter 1 (SNAT1) expression in piglet pulmonary artery endothelial cells. Am J Physiol Heart Circ Physiol. 2019 Apr 1;316(4):H911-H919. doi: 10.1152/ajpheart.00674.2018. Epub 2019 Feb 22. PMID: 30794434; PMCID: PMC6483017

This work led to translational research efforts to develop novel therapies to treat infants with chronic and progressive forms of pulmonary hypertension (PH) associated with conditions such as bronchopulmonary dysplasia. Based on our laboratory work, we hypothesized that L-citrulline would be an effective precursor for endogenous NO production and a novel therapy for progressive forms of neonatal PH. This work was supported by several complementary grants from NHLBI. U01HL101456 (PI: J Aschner) was a clinical study in extremely premature infants to examine biomarkers of biochemical immaturity and functional genetic variation in the urea cycle-NO pathway. R01 HL097566 and R56 HL097566 (PI: C. Fike, co-investigator: J Aschner) examines citrulline uptake and metabolism and its effects on NO production, NOS uncoupling and pulmonary vascular responses in a newborn pig model of chronic hypoxia-induced PH and the efficacy of citrulline and tetrahydrobiopterin (BH4) therapy to ameliorate PH. This highly translational work has culminated in a number of important publications and a patient focused research grant (NIH R34 HL142995), “Pharmacokinetics and safety of oral L-citrulline in infants with bronchopulmonary dysplasia” This is a phase 1 study to characterize the pharmacokinetic profile of oral L-citrulline in preterm infants at high risk for developing BPD-PH and to evaluate the safety, tolerability, and ability to achieve target L-citrulline plasma levels of 100-150 uM in patients at high risk of developing BPD-PH treated for 48 hours with oral L-citrulline.

a. Vadivel A, **Aschner JL**, Rey-Parra GJ, Magarik J, Zeng H, Summar M, Eaton F, Thebaud B. L-citrulline attenuates arrested alveolar growth and pulmonary hypertension in oxygen-induced lung injury in newborn rats. *Pediatr Res.* 2010 Dec;68(6):519-525. PMCID: PMC3132222

b. Fike CD, Summar M, **Aschner JL**. L-citrulline provides a novel strategy for treating chronic pulmonary hypertension in newborn infants. *Acta Paediatr.* 2014 Oct;103(10):1019-1026. PMCID: PMC4209175

c. Fike CD, Dikalova A, Kaplowitz MR, Cunningham G, Summar M, **Aschner JL**. Rescue Treatment with L-Citrulline Inhibits Hypoxia-Induced Pulmonary Hypertension in Newborn Pigs. *Am J Respir Cell Mol Biol.* 2015 Aug;53(2):255-264. PMCID: PMC4566047

d. **Aschner J**, Avachat C, Birnbaum A, Sherwin C, Fike C. Multi-dose enteral L-citrulline administration in premature infants at risk of developing pulmonary hypertension associated with bronchopulmonary dysplasia. Res Sq. 2023 Jun 9:rs.3.rs-3006963. doi: 10.21203/rs.3.rs-3006963/v1. PMID: 37333204; PMCID: PMC10275028.

C.2. The Prematurity and Respiratory Outcomes Program (PROP)

This U01 study examined molecular and genetic biomarkers in the urea cycle-NO and oxidant-antioxidant pathways of preterm infants at risk for BPD and long-term respiratory morbidity. I served as contact PI of the Vanderbilt PROP study and a member of the PROP Steering Committee, Biospecimen’s Committee, Publication Committee, PROP Scholar’s Committee, and Chair of the PROP Budget Committee. The following selected publications were supported by PROP funding.

a. Poindexter BB, Feng R, Schmidt B, **Aschner JL**, Ballard RA, Hamvas A, Reynolds AM, Shaw PA, Jobe AH, Prematurity, Respiratory Outcomes P. Comparisons and Limitations of Current Definitions of Bronchopulmonary Dysplasia for the Prematurity and Respiratory Outcomes Program. *Ann Am Thorac Soc.* 2015 Dec;12(12):1822-1830. PMCID: PMC4722827

b. Keller RL, Feng R, DeMauro SB, Ferkol T, Hardie W, Rogers EE, Stevens TP, Voynow JA, Bellamy SL, Shaw PA, Moore PE; Prematurity and Respiratory Outcomes Program. Bronchopulmonary Dysplasia and Perinatal Characteristics Predict 1-Year Respiratory Outcomes in Newborns Born at Extremely Low Gestational Age: A Prospective Cohort Study. J Pediatr. 2017 doi: 10.1016/j.jpeds.2017.04.026. PMID: 28528221; PMCID: PMC5533632

c. O'Connor MG, Suthar D, Vera K, Slaughter JC, Maitre NL Steele S, Beller A, Fike CD, **Aschner JL**, Moore PE, Austin ED. Pulmonary Hypertension in the Premature Infant Population: Analysis of Echocardiographic Findings and Biomarkers. Pediatr Pulmonol. 2018 Mar;53(3):302-309. doi: 10.1002/ppul.23913. Epub 2017 Nov 23. PMID:29168320; PMCID: PMC5815883
d. Hamvas A, Feng R, Bi Y, Wang F, Bhattacharya S, Mereness J, Kaushal M, Cotten CM, Ballard PL, Mariani TJ; **PROP Investigators**. Exome sequencing identifies gene variants and networks associated with extreme respiratory outcomes following preterm birth. *BMC Genet*. 2018 Oct 20;19(1):94. doi: 10.1186/s12863-018-0679-7. PMID: 30342483; PMCID: PMC6195962

C.3 Environmental Health Research

I have a long-standing interest in environmental health research with both basic and clinical/translational research grant funding from NIEHS and publications focusing on the developmental neurotoxicology of metals, particularly manganese (Mn). I am MPI of the longitudinal preterm cohort study "Developmental Impact of NICU Exposures (DINE), part of the Environmental Influences on Child Health Outcomes (ECHO) program (UH3OD02332). ECHO is a 14-year initiative to investigate a broad range of exposures that can impact children's long-term health. The DINE study investigates exposures in Neonatal Intensive Care Units (NICU) to chemicals, such as phthalates, which are used in plastic medical equipment, and their association with adverse health outcomes in childhood.

Selected environmental health publications (from more than 30) include:

a. **Aschner JL**, Anderson A, Slaughter JC, Aschner M, Steele S, Beller A, Mouvery A, Furlong HM, Maitre NL. Neuroimaging identifies increased manganese deposition in infants receiving parenteral nutrition. *Am J Clin Nutr.* 2015 Dec;102(6):1482-1489. PMCID: PMC4658463
b. Stroustrup, A, Teitelbaum, S, **Aschner JL**. The Canary in the Coal Mine: The Value of Preterm Infant Environmental Health Cohorts. *JAMA Pediatrics* 2017 Dec 1;171(12):1139-1140. doi: 10.1001/jamapediatrics.2017.3230. PMID:29059271
c. O'Shea TM, McGrath M, **Aschner JL**, Lester B, Santos HP Jr, Marsit C, Stroustrup A, Emmanuel C, Hudak M, McGowan E, Patel S, Fry RC; program collaborators for Environmental influences on Child Health Outcomes. Environmental influences on child health outcomes: cohorts of individuals born very preterm. *Pediatr Res*. 2022 Aug 10:1-16. doi: 10.1038/s41390-022-02230-5. Online ahead of print. PMID: 35948605
d. Stroustrup A, Zhang X, Spear E, Bandyopadhyay S, Narasimhan S, Meher AK, Choi J, Qi G, Poindexter BB, Teitelbaum SL, Andra SS, Gennings C, **Aschner JL**. Phthalate exposure in the neonatal intensive care unit is associated with development of bronchopulmonary dysplasia. Environ Int. 2023 Aug;178:108117. doi: 10.1016/j.envint.2023.108117. Epub 2023 Jul 26. PMID: 37517179; PMCID: PMC10581357.

Complete List of Published Work in MyBibliography:
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