BIOGRAPHICAL SKETCH

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NAME: MacFarlane, Peter

eRA COMMONS USER NAME (credential, e.g., agency login): macfarlane1

POSITION TITLE: Assistant Professor

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)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
LaTrobe University, Melbourne	BS	03/1995	11/1998	Biological Science
LaTrobe University, Melbourne	PHD	01/1999	10/2004	Zoology
University of Wisconsin, Madison	Postdoctoral Fellow	03/2005	03/2011	Respiratory Neurobiology

A. Personal Statement

As Assistant Professor in the Department of Pediatrics, CWRU and Rainbow Babies & Children's Hospital (RB&C), I have developed an independent research lab focused on the developing respiratory system and how it is affected by early life experiences. I have a particular interest in how components of the extracellular matrix (such as hyaluronan), modulate development of the respiratory system. Much of my research is centered on the types of scenario's or conditions commonly faced by preterm infants. Ongoing studies focus on determining the pathophysiology associated with Sudden Infant Death Syndrome, neonatal continuous positive airway pressure (CPAP), apnea of prematurity, and supplemental oxygen therapy. The overall hypothesis driving my research is that early life experiences, particularly during uniquely vulnerable periods of development, may underlie various forms of respiratory morbidities later in life. We hope that an understanding of the interactions between these early life experiences and the developing respiratory system may help to refine current treatment, or guide the development of new therapeutic interventions used in the care of (particular preterm) infants. The lab is currently funded by two R01's, a foundation grant, and I serve as co-investigator on several others.

1. Bavis RW, MacFarlane PM. Developmental plasticity in the neural control of breathing. Exp. Neurol. 2017; 287(Pt 2):176-191. PubMed PMID: PMID: 27246998.
2. Mayer CA, Di Fiore JM, Martin RJ, Macfarlane PM. Vulnerability of neonatal respiratory neural control to sustained hypoxia during a uniquely sensitive window of development. J Appl Physiol (1985). 2014 Mar 1;116(5):514-21. PubMed PMID: 24371020.
3. MacFarlane PM, Ribeiro AP, Martin RJ. Carotid chemoreceptor development and neonatal apnea. Respir Physiol Neurobiol. 2013 Jan 1;185(1):170-6. PubMed PMID: 22842008.
4. Mayer CA, Martin RJ, MacFarlane PM. Increased airway reactivity in a neonatal mouse model of continuous positive airway pressure. Pediatr Res. 2015 Aug;78(2):145-51. PubMed PMID: 25950451; PubMed Central PMCID: PMC4506702.

B. Positions and Honors

Positions and Employment

1999 - 2004 PhD., LaTrobe University, Melbourne
2004 - 2005 Research Assistant, University of Melbourne/Howard Florey Institute, Melbourne
2005 - 2011 Postdoctoral Fellow, University of Wisconsin, Madison, WI
2011 - Asst. Professor, Case Western Reserve University/Rainbow Babies & Children's Hospital, Cleveland, OH

Honors

1999	First Class Honors, Bachelor of Science, LaTrobe University, Melbourne, Australia
1999	Summer Research Scholarship, LaTrobe University, Melbourne, Australia
2000	Australian Postgraduate Award, LaTrobe University, Melbourne, Australia
2008	Parker B. Francis Fellowship, Francis Family Foundation
2010	Carolyn-Tum Suden Hillebrandt Award, Experimental Biology Meeting

C. Contribution to Science

1. My lab recently developed a neonatal rodent model of sudden infant death syndrome that exhibits all of the hallmarks of a SIDS-related event including: 1) vulnerability to hypoxia exposure; 2) a critical window of development; 3) brainstem abnormalities in serotonin expression; and 4) changes in brainstem microglia expression. We have identified a possible cause of the vulnerability, which describes a disturbance in key neurodevelopmental events that are necessary for cardio-respiratory control.
   a. Stryker C, Camperchioli DW, Mayer CA, Alilain WJ, Martin RJ, MacFarlane PM. Respiratory dysfuncti0n following neonatal sustained hypoxia exposure during a critical window of brainstem extracellular matrix formation. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2018; 314(2):R216-227. PubMed PMID: 29046314.
   b. Rourke KS, Mayer CA, MacFarlane PM. A critical postnatal period of heightened vulnerability to lipopolysaccharide. Respir Physiol Neurobiol. 2016 Oct;232:26-34. PubMed PMID: 27328410.
   c. MacFarlane PM, Mayer CA, Litvin DG. Microglia modulate brainstem serotonergic expression following neonatal sustained hypoxia exposure: implications for sudden infant death syndrome. J Physiol. 2016 Jun 1;594(11):3079-94. PubMed PMID: 26659585; PubMed Central PMCID: PMC4887678.
   d. Mayer CA, Di Fiore JM, Martin RJ, Macfarlane PM. Vulnerability of neonatal respiratory neural control to sustained hypoxia during a uniquely sensitive window of development. J Appl Physiol (1985). 2014 Mar 1;116(5):514-21. PubMed PMID: 24371020.

2. My lab also developed the first neonatal mouse model of continuous positive airway pressure (CPAP). We use this to model CPAP administration to preterm infants to assess its effects on airway hyper-reactivity. With this new technology developed in my lab to administer CPAP to a neonatal mouse without the use of anesthesia or major surgical preparation, we are beginning to open possibilities toward understanding how CPAP (independently of hyperoxia) modifies lung development.
   a. Mayer CA, Martin RJ, MacFarlane PM. Increased airway reactivity in a neonatal mouse model of continuous positive airway pressure. Pediatr Res. 2015 Aug;78(2):145-51. PubMed PMID: 25950451; PubMed Central PMCID: PMC4506702.
   b. Reyburn B, Di Fiore JM, Raffay T, Martin RJ, Prakash YS, Jafri A, MacFarlane PM. The Effect of Continuous Positive Airway Pressure in a Mouse Model of Hyperoxic Neonatal Lung Injury. Neonatology. 2016;109(1):6-13. PubMed PMID: 26394387; PubMed Central PMCID: PMC4654984.

3. Elucidated several important signaling molecules involved in spinal mechanisms of respiratory plasticity following intermittent hypoxia exposure in adult rats.
   a. MacFarlane PM, Satriotomo I, Windelborn JA, Mitchell GS. NADPH oxidase activity is necessary for acute intermittent hypoxia-induced phrenic long-term facilitation. J Physiol. 2009 May 1;587(Pt 9):1931-42. PubMed PMID: 19237427; PubMed Central PMCID: PMC2689334.
   b. MacFarlane PM, Mitchell GS. Episodic spinal serotonin receptor activation elicits long-lasting phrenic motor facilitation by an NADPH oxidase-dependent mechanism. J Physiol. 2009 Nov 15;587(Pt 22):5469-81. PubMed PMID: 19805745; PubMed Central PMCID: PMC2793877.
   c. MacFarlane PM, Vinit S, Mitchell GS. Serotonin 2A and 2B receptor-induced phrenic motor facilitation: differential requirement for spinal NADPH oxidase activity. Neuroscience. 2011 Mar 31;178:45-55. PubMed PMID: 21223996; PubMed Central PMCID: PMC3072788.

d. MacFarlane PM, Vinit S, Mitchell GS. Spinal nNOS regulates phrenic motor facilitation by a 5-HT2B receptor- and NADPH oxidase-dependent mechanism. Neuroscience. 2014 Jun 6;269:67-78. PubMed PMID: 24680940; PubMed Central PMCID: PMC4361021.

4. Characterized the respiratory neurobiology and of newborn marsupials. After as little as a 10 days gestation (in some species), the marsupial is born at a very altricial stage of development. The lungs resemble simple air sacs and are not able to support the metabolic needs of the neonate. Instead, these minute marsupials depend heavily on the skin for the exchange of O2 and CO2 during the first weeks of postnatal life. During the transition from skin-to-lung exchange, the lungs mature as respiratory mechanics and the energetics of breathing improve, and various reflexes controlling breathing become robust, including the Hering-Breuer inflation reflex and the hypoxic and hypercapnic ventilatory response.

   e. MacFarlane PM, Frappell PB. Convection requirement is established by total metabolic rate in the newborn tammar wallaby. Respir Physiol. 2001 Jul;126(3):221-31. PubMed PMID: 11403784.

   f. MacFarlane PM, Frappell PB, Mortola JP. Mechanics of the respiratory system in the newborn tammar wallaby. J Exp Biol. 2002 Feb;205(Pt 4):533-8. PubMed PMID: 11893767.

   g. MacFarlane PM, Frappell PB. Hypothermia and hypoxia inhibit the Hering-Breüer reflex in the marsupial newborn. Am J Physiol Regul Integr Comp Physiol. 2004 May;286(5):R857-64. PubMed PMID: 14695112.

   h. Frappell PB, MacFarlane PM. Development of the respiratory system in marsupials. Respir Physiol Neurobiol. 2006 Nov;154(1-2):252-67. PubMed PMID: 16781204.

Complete List of Published Work in My Bibliography:
http://bit.ly/1kDcVGZ

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Gerber Foundation
MacFarlane (PI)
06/01/15-06/01/18
Myo-inositol for the treatment and prevention of apnea of prematurity: bench to bedside
The primary purpose of this proposal is to determine whether myo-inositol supplementation reduces apnea incidence in rodent model of apnea of prematurity. This proposal also combines an ancillary clinical trial to test the effects of myo-inositol supplementation on the incidence of intermittent hypoxia in preterm infants.
Role: PI

R01 HL056470-15 (NCE), NIH
MacFarlane (Co-PI)
12/01/16-11/30/20
Neonatal Modulation of Airway Contractility
The major goal of this project is to determine the contribution of brain-derived neurotrophic factor in hyperoxia induced enhancement of airway smooth muscle Ca2+ and contractility, as it relates to neonatal asthma.
Role: PI (CWRU site)

R01 HL 138402-01, NIH
MacFarlane (PI)
07/01/17-06/30/22
Understanding CPAP effects on developing airway
The major goal of this project is to characterize the role of hyaluronan signaling in airway reactivity in a mouse model of neonatal continuous positive airway pressure (CPAP).
Role: PI

U01 RES208928, NIH
Hibbs, Martin [multiple PIs] (PI)
01/01/16-01/01/21
Prematurity Related Ventilatory Control - Clinical Research Center
The purpose of this project is to establish the contribution of impaired respiratory control on the continuing long term morbidity of former preterm infants.
Role: Co-Investigator

CBR-Cord Blood Registry
Bonfield (PI)
03/15/2017-03/14/2018
Cord Tissue Derived Mesenchyma Stem Cells to Reverse or Improve the Outcome in Murine Model of Cystic Fibrosis and Optimization of Culture Conditions to Maximize Potency and Efficacy.
The major goal of this project is to characterize the role of mesenchymal stem cell signaling in airway reactivity in mouse models of cystic fibrosis.
Role: Co-Investigator