BIOGRAPHICAL SKETCH

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NAME: Jihan K. Osborne

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POSITION TITLE: Assistant Professor - Department of Pharmacology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Saint Francis College Brooklyn, New York	B.S.	05/2003	Biology and Chemistry
University of Texas Southwestern Medical Center, Dallas, Texas	Ph.D.	05/2013	Cell and Molecular Biology
Harvard Medical School/ Boston Children's Hospital Boston, Massachusetts	Post-Doctoral	08/2019	Developmental Biology

A. Personal Statement

The future of translational biomedical research lies in the ability of investigators to attack scientific problems from multiple perspectives and disciplines. My scientific background is comprised of many areas of expertise gained from time spent in several different laboratories including: developmental biology, neuroscience, stem cell biology, pharmacology/cell signaling and most important to the future of my lab, cancer biology. My experience in these laboratories led me to develop a complicated curiosity for how gene regulatory programs and signaling pathways required for development are used and paralleled during tumor initiation and metastasis. I will continue to develop this curiosity into a research program in my own laboratory. My expertise, determination and training for the past +15 years has prepared me not only scientifically for the task ahead of running a compelling, impactful and strong academic research laboratory but also for the influence my success will have on the younger generation of black and brown female scientist. I have faced many challenges, but with each momentary set-back I learned to approach my scientific and personal endeavors more aware, more creative, and more independent.

After receiving my bachelor's, I was awarded a post-baccalaureate scholarship at the National Institutes of Health in the National Institute of Aging. I worked on two congruent projects, first confirming Sox2 as a marker of adult/aging neural stem cells in human and murine neurospheres, then using a Sox2-GFP mouse model in a mouse model of Alzheimer's disease. This experience unlocked my interest in understanding the role of developmental programs in disease. During graduate school I worked on Neurogenic differentiation1 (NeuroD1), a bHLH transcription factor responsible for neuronal and neuroendocrine differentiation during organogenesis of the central and peripheral nervous system and the pancreas respectively. I discovered that NeuroD1 was more highly expressed in a subset of aggressive human SCLC lung cancer cell lines as compared to non-aggressive human SCLC lung cancer, non-SCLC (NSCLC) and normal immortalized human bronchial epithelial (HBECs) cell lines. Loss of NeuroD1 in human SCLC cell lines led to decreased survival and metastatic capability of SCLC cells; whereas overexpression in HBECs and NSCLC cells led to increased migratory potential. Downstream targets responsible for the increased migration were the co-regulation of the receptor tyrosine kinase (TrkB) and the neural adhesion molecule (NCAM) by NeuroD1.

During my post-doctoral fellowship with Dr. George Daley at Boston Children's Hospital/Harvard Medical

School, I investigated the role of the RNA-binding proteins, Lin28a and Lin28b, during mammalian kidney and lung development. Lin28 proteins are highly expressed in mouse and human embryonic stem cells and are ubiquitously expressed throughout the mouse embryo with their expression declining early-mid gestation. In the kidney, we found that the Lin28/*let-7* axis regulates the timing of branching morphogenesis and nephrogenesis via control of Igf2 mRNA. Another key organ where branching morphogenesis dictates complexity is lung. Loss of the Lin28 paralogs in the embryonic lung epithelium led to a delay in branching morphogenesis subsequently followed by aberrant bronchiolar and alveolar differentiation, which eventually led to perinatal lethality. During development of several tissues (including the lung and kidney) expression of the Lin28 paralogs are inversely associated with their downstream targets the miRNA family of *let-7*. We and others have shown that the Lin28 proteins inhibits the maturation of *let-7*, while Lin28 itself is a target of *let-7*. I determined that during early lung and kidney development the family of mature *let-7* miRNAs were not expressed until mid-late gestation. Mechanistically, I found that Lin28 was able to bind directly to and control the expression of several master regulators of branching morphogenesis and cell fate, such as *Sox2, Sox9*, and *Etv5* particularly in the lung, kidney, and brain. The work done during my graduate and post-doctoral studies have left me with many questions about the role of developmental programs during the transitions from embryogenesis into adulthood and throughout oncogenesis. These questions range from a deeper understanding of the pathways that regulate homeostasis during these developmental transitions to deciphering their innate contributions to disease, particularly oncogenic transformation and metastasis.

B. Positions and Honors

Positions

2020- pres. Assistant Professor- University of Texas Southwestern Medical Center

2019-2020 Research Scientist- The Broad Institute of Harvard and MIT

2013-2019 Post-Doctoral Fellow- Laboratory of George Daley (Selected for National Heart, Lung and Blood Institute/NHLBI Training Grant)

2006-2013 Graduate Student- Laboratory of Melanie Cobb (Selected for National Institute of General Medicine/NIGMS Pharmacological Sciences Training Grant)

Honors

2003 National Institutes of Health (NIH) /National Institute of Aging (NIA) IRTA (Intramural Research Training Award) Fellowship (2003-2005)

2010 National Institutes of General Medical Sciences (NIGMS) Pharmacological Sciences Training Grant 5-T32 GM007062 (2010-2013)

2016-2019. Burroughs Wellcome Fund-Postdoctoral Award (2016-2019)

C. Contributions to Science

1) The function of developmental neurogenic bHLH transcription factors in small cell lung cancer

I demonstrated that expression of NeuroD1 in aggressive small cell lung cancer (SCLC) and neuroendocrine cell lines led increased migratory potential through up regulation TrkB and NCAM, both druggable targets. This work resulted in three first authored manuscripts. Additionally, I examined the differences between ASCL1(another lineage-restricted bHLH transcription factor that is overexpressed in SCLC) and NeuroD1, demonstrating that NeuroD1 is be expressed in more metastatic SCLC than ASCL1.

PUBLICATIONS

Osborne JK, Larsen JE, Shields MD, KulKarni A, Gonzales, JX, Girard, L, Shames DS, Sato, M, Minna JD, Cobb MH *NeuroD1 Regulates Survival and Migration of Neuroendocrine Lung Carcinomas via Signaling Molecules TrkB and NCAM* **PNAS**, 2013 110 6524-9

Osborne JK, Larsen JE, Gonzales JX, Girard L, Shames DS, Sato M, Minna JD, Cobb MH *NeuroD1 regulation of migration of accompanies differential sensitivity of neuroendocrine carcinomas to TrkB Inhibition* **ONCOGENESIS**; 2013 2: e63.

Osborne JK, Guerra ML, Gonzales JX, McMillan EA, Minna JD, Cobb MH *NeuroD1 mediates nicotine-induced migration and invasion via regulation of the nicotinic acetylcholine receptor subunits in a subset of neural and neuroendocrine carcinomas* **MBoC** 2014 25:11 1782-1792 doi:10.1091/mbc. E13-06-0316.

Borromeo MD, Savage TK, Kollipara RK, He M, Augustyn A, **Osborne JK**, Girard L, Minna JD, Gazdar AF, Cobb MH, Johnson JE *ASCL1 and NEUROD1 Reveal Heterogeneity in Pulmonary Neuroendocrine Tumors and Regulate Distinct Genetic Programs.* **Cell Reports**. 2016 Aug 2;16(5):1259-1272.

2) The role of LIN28/*LET-7* axis during branching morphogenesis of Kidney and Lung

Together with my colleague we revealed how the Lin28/Let7 axis regulated branching morphogenesis during embryonic development of the mammalian lung, kidney, and brain. This work resulted in a patent, a co-first authored manuscript published in Nature Communications and another currently under review. Critical because babies that are born prematurely have under developed lung and kidneys leading to lifelong complications such as diabetes, while current therapies are inadequate broad acting steroids.

PATENTS

Yermalovich, AV **Osborne JK**, Daley GQ. Enhanced organogenesis through manipulation of Lin28/*let*-7/Dis3L2. Patent WO2018/232191.

PUBLICATIONS

Osborne JK, Kinney MA, Han A, Akinnola KE, Vo LT, Yermalovich AV, Sousa PM, Pearson DS, Barragan J, Metzger, RJ, Daley GQ *Lin28 paralogs regulate developmental timing in embryonic lung epithelial progenitors. (*Manuscript under review at Cell Reports).

Osborne JK, Lummertz da Rocha E, Gupta M, Sousa PM, Yermalovich AV, Brainson CF, Rowe RG, Jha D,, Barragan J, Kim CF, Daley GQ *Transcriptional and posttranscriptional regulation of oncofetal programs during development and tumorigenesis.* (Manuscript in preparation).

2019 - Yermalovich AV^, **Osborne JK^**, Sousa PM, Han A, Kinney MA, Chen MJ, Robinton D, Montie H, Pearson DS, Wilson SB, Combes AN, Little MH*, Daley GQ *. *Lin28/let-7 Regulates the Timing of Cessation of Nephrogenesis.* **Nat Comm.** 2019 Jan 11; 10(1): 168**.** ^ Co-first authorship

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

<u>Pending Support</u>

Cancer Prevention and Research Institute of Texas (CPRIT) Research Scholar