### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.** 

#### NAME: Liu, Ning

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

POSITION TITLE: Assistant Professor of Molecular Biology and Hamon Center for Regenerative Science and 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<br>(if<br>applicable) | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY    |
|--|------------------------------|-------------------------------|-------------------|
| University of Science and Technology of China,<br>Hefei, China           | BS                           | 1995                          | Biology           |
| University of Wisconsin, Madison, Wisconsin                              | PhD                          | 2003                          | Cancer Biology    |
| University of Texas Southwestern Medical Center at Dallas, Dallas, Texas | Postdoctoral fellow          | 2004-2009                     | Molecular Biology |

### A. Personal Statement

I study the molecular mechanisms of skeletal muscle development, function and disease. As a postdoctoral fellow with Dr. Eric Olson, I studied the roles of transcription factor Hand2 and microRNA miR-133 in controlling heart development and function. I also identified 2 muscle specific microRNAs as key regulators of muscle diseases such as centronuclear myopathy and Duchenne Muscular Dystrophy. Recently, I have focused my research on transcriptional regulation of skeletal muscle regeneration and disease. I also identified a novel myogenic progenitor that contributes to skeletal muscle. Over the past decade, I have published 27 publications, 14 as first authors, 4 as co-corresponding authors, and 2 as corresponding authors.

As an Assistant Professor of Molecular Biology, my lab focuses on defining the molecular pathways that regulate cardiac and skeletal muscle development and disease. Our long-term goal is to delineate the signaling pathways for the formation and function of striated muscle and to use this information to design pharmacologic and genetic therapies for inherited and acquired striated muscle diseases in humans.

### **B.** Positions and Honors

### **Positions/Employment**

1998-2003Graduate student with Dr. Daniel Loeb, University of Wisconsin, Madison, WI2004-2008Postdoctoral fellow with Dr. Eric Olson, UT Southwestern Medical Center, Dallas, Texas2009-2012Instructor of Molecular Biology, UT Southwestern Medical Center, Dallas, Texas2012-presentAssistant Professor of Molecular Biology, UT Southwestern Medical Center, Dallas, Texas2014-presentAssistant Professor, Hamon Center for Regenerative Science and Medicine, UT Southwestern

### Honors and Awards

2005-2007 Pollin Research Award for Young Investigators

# C. Contribution to Science

I have studied the molecular mechanisms that control heart and skeletal muscle development, function and disease. Here is a summary of some of my work:

**I. A novel myogenic progenitor that contributes to adult skeletal muscle.** We recently identified a Twist2depedent progenitor in adult skeletal muscle that contributes specifically type IIb myofibers. These progenitor cells are distinct from Pax7 satellite cells and are myogenic in vitro and in vivo. They contribute to maintenance of type IIb myofiber size during aging. We are currently focusing on understanding the mechanism of action of Tw2 cells and the functions of the Tw2 transcription factor in controlling cell fate.

 Liu N\*, Garry GA, Li S, Bezprozvannaya S, Sanchez-Ortiz E, Chen B, Shelton JM, Jaichander P, Bassel-Duby R, Olson EN\*. "A Twist2-dependent progenitor cell contributes to adult skeletal muscle". Nat Cell Biol. 2017 19(3):202-213. \*Corresponding authors

**II. Transcriptional Regulation of skeletal muscle development and regeneration:** I have been interested in understanding how transcription factors control muscle development and adult muscle regeneration. Adult skeletal muscle has remarkable capacity to regenerate due to the existence of muscle stem cells (satellite cells). Much of my research is also focused on studying transcription factors, microRNAs and signaling pathways that regulate satellite cell proliferation and differentiation.

- 1. Cenik BK, Liu N, Chen B, Bezprozvannaya S, Olson EN, Bassel-Duby R. "Myocardin-related transcription factors are required for skeletal muscle development". **Development.** 2016 Jul 6. pii: dev.135855.
- Liu N\*, Nelson BR, Bezprozvannaya S, Shelton JM, Richardson JA, Bassel-Duby R, Olson EN\*. "Requirement of MEF2A, C, and D for skeletal muscle regeneration." Proc Natl Acad Sci U S A. 2014. 111(11):4109-14. \*Corresponding authors
- Liu N\*, Williams A.H., Maxeiner J.M., Bezprozvannaya S., Shelton J.M., Richardson J.A., Bassel-Duby R., Olson E.N. \* 2012. "MicroRNA-206 promotes skeletal muscle regeneration and delays progression of Duchenne muscular dystrophy in mice. *J Clin Invest.* 122 (6):2054-2065.\*Corresponding authors

**III. Molecular mechanisms of congenital myopathies:** Congenital myopathies, such as Nemaline myopathy and centronuclear myopathy, are caused by genes encoding sarcomeric proteins. I have a long-term interest in understanding the molecular mechanisms of these disease. In particular, I am interested in how proteins such as Leomodin-3 and Kelch proteins maintain sarcomere integrity and how mutations in these proteins cause Nemaline myopathy. In addition, I am interested in how studying the role of microRNAs in regulating centronuclear myopathy.

- 1. Cenik BK, Garg A, Shelton JM, Richardson JA, Bassel-Duby R, Olson EN<sup>\*</sup>, Liu N<sup>\*</sup>. "Leiomodin-3 Acts Within an SRF/MEF2-Dependent Transcriptional Regulatory Circuit to Maintain Sarcomere Integrity and Skeletal Muscle Function". J Clin Invest. 2015;125:1569-1578. \*Corresponding authors
- Liu N\*., Bezprozvannaya S., Shelton J.M., Frisard M.I., Hulver M.W., McMillan R.P., Wu Y., Voelker K.A., Grange R.W., Richardson J.A., Bassel-Duby R., Olson E.N.\* 2011. Mice lacking microRNA 133a develop dynamin 2-dependent centronuclear myopathy. *J Clin Invest.* 121 (8): 3258–3268. Corresponding authors
- Anderson DM, Cannavino J, Li H, Anderson KM, Nelson BR, McAnally J, Bezprozvannaya S, Liu Y, Lin W, Liu N, Bassel-Duby R, Olson EN. "Severe muscle wasting and denervation in mice lacking the RNA-binding protein ZFP106". Proc Natl Acad Sci U S A. 2016 Jul 14. pii: 201608423.

**IV. Molecular pathways mediating heart development, function and heart disease:** My research focuses on delineating how transcription factors and microRNAs control heart formation and how perturbation of the gene regulatory network causes cardiac remodeling leading to heart disease. Our goal is t to develop new therapies to combat heart disease, the leading cause of mortality in the world.

- 1. Liu N., Barbosa A.C., Qi X., Bezprozvannaya S., Richardson J.A., Chapman S.L., Yanagisawa H. and Olson E.N. 2009. DNA binding-dependent and –independent functions of the Hand2 transcription factor during mouse embryogenesis. **Development** 136:933-942.
- Liu N., Bezprozvannaya S., Williams A.H., Qi X., Richardson J.A., Bassel-Duby R., Olson E.N. 2008. microRNAs-133a regulates cardiomyocyte proliferation and suppresses smooth muscle gene expression in the heart. Genes Dev 22: 3242-3254.
- Liu N., Williams A.H., Kim Y., McAnally J., Bezprozvannaya S., Sutherland L.B., Richardson J.A., Bassel-Duby R. and Olson E.N. 2007. An intragenic MEF2-dependent enhancer directs muscle-specific expression of microRNAs 1 and 133. Proc Natl Acad Sci U S A. 104:20844-20849.
- Liu N., Olson E.N. 2010. MicroRNA regulatory networks in cardiovascular development. Dev Cell. 18 (4):510-525.

# Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/46828208/?sort=date&direction=ascending

#### D. RESEACH SUPPORT Ongoing Research Support

None

# **Completed Research Support**

Beginning Grant-in-Aid from American Heart Association SouthWest Affiliate AHA15BGIA25830014 Liu (PI) 07/01/2015-06/30/2017 Title: Role of Twist-2 positive progenitor cells in adult heart regeneration The goal of this project to characterize a novel Twist-2-dependent cardiac progenitor cell and understand its contribution to cardiomyocytes, fibroblasts and endothelial cells during adult heart remodeling and regeneration. Role: PI

Beginning Grant-in-Aid from American Heart Association SouthWest Affiliate AHA13BGIA17150004 Liu (PI) 07/01/2013-06/30/2015 Title: Cardiac repair and regeneration by Twist-1 and Twist-2. The goal of this project is to explore the functions of transcription factors Twist-1 and Twist-2 in controlling cardiac repair and regeneration, and to uncover new disease mechanisms and therapeutic approaches for heart disease.

Role: PI

Scientist Development Grant from American Heart Association National CenterAHA09SDG2310201Liu (PI)07/01/2009-06/30/2013Title: microRNAs regulation of cardiac stem cells during regeneration and repair.The goal of this project is to study the role of microRNAs such as miR-133a in regulating adult cardiac stemcell fates during regeneration and repair.Role: PI

2007-2009

Post-doctoral fellowship from American Heart Association AHA0725178Y Liu (postdoc fellow) 07/0 Title: Role of miR-133a in heart development.

07/01/2007-06/30/2009

The goal of this project is to study the role of microRNAs 133a during heart development and disease.

Role: Postdoctoral fellow