BIOGRAPHICAL SKETCH

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NAME: Shi, Fubiao

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

POSITION TITLE: Postdoctoral Research Fellow

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)	Completion Date MM/YYYY	FIELD OF STUDY
Huazhong Agricultural University, Wuhan, China	BS	09/2002-06/2006	Biological Sciences
Fudan University, Shanghai, China	PHD	09/2006-06/2014	Developmental Biology
Sanford Burnham Prebys Medical Discovery Institute at Lake Nona, Orlando, Florida	Postdoctoral Associate	08/2014-12/2017	Metabolic Disease and Signaling
Vanderbilt University Medical Center, Division of Cardiovascular Medicine, Nashville, Tennessee	Postdoctoral Fellow	01/2018-present	Metabolic Disease and Signaling

A. Personal Statement

Biomedical research, especially the field of metabolic disease studies, has always been an inspiration to me. All the efforts of my research aim to provide valuable knowledge for the development of novel therapies to treat obesity, diabetes and related metabolic disorders.

My academic training has provided me with a strong background in several related areas. As an undergraduate major in biological sciences, my thesis project aimed to investigate the association between obesity and the single nucleotide polymorphism of SOCS3 gene in Chinese populations. This project raised my original interest in the metabolic field. My graduate study is in the field of mouse genetics and developmental biology. My Ph.D. training was supervised by Dr. Xiaohui Wu at Fudan University, Shanghai, China. My dissertation project established a piggyBac insertional mouse model of BPES syndrome, an autosomal dominant genetic disorder in humans, revealed the crucial role of the transcription factor Foxl2 in mouse midface development and suggested a long-range regulation of Foxl2 craniofacial expression by an evolutionarily conserved distal enhancer. Through this project, I gained extensive training and mastered a variety of hands-on techniques of mouse genetics, cellular, molecular, and developmental biology and the methodology to investigate gene regulation. For postdoctoral training, I joined Dr. Sheila Collins's laboratory at Sanford Burnham Prebys Medical Discovery Institute at Lake Nona to study adipose tissue biology. My project aims to a) investigate the roles of natriuretic peptide clearance receptor NPRC in modulating NP-mediated metabolism in adipose tissues and skeletal muscles, and b) understand the transcriptional regulation of natriuretic peptide receptor gene expression in adipose tissue by nutritional and environmental cues. During the last two years of postdoc training, I have acquired rather sound experiences in adipose tissue biology and metabolic studies including using cell and mouse models in combination with cellular, molecular, functional genomic and integrative metabolic approaches.

My long-term goal is to elucidate the metabolic effects of natriuretic peptides in peripheral organs and to delineate the broader signaling pathways that are critical for adipose browning and energy expenditure by using a combination of cell and mouse models, cellular and molecular mechanisms, and functional genomic approaches. The proposed study will be a valuable training opportunity and will provide necessary and new skills for future studies and enable me to develop critical thinking and collaborative research projects. Following my postdoctoral training, I plan to transition toward an independent research scientist position either in an academic institute or in an industrial company. My research interests will continue to focus on metabolic disease, especially on obesity, diabetes and related metabolic disorders, with a translational orientation for new therapeutics. I believe that receiving this postdoctoral fellowship award will be extremely beneficial for my postdoctoral training and will be a great leap forwards for my future career as a mature scientist in the field.

B. Positions and Honors

Positions and Employment

2005.09 - 2006.02 Undergraduate research assistant, Huazhong Agricultural University, Wuhan,China
2006.03 - 2006.07 Visiting undergraduate student, Fudan University, Shanghai,China
2008.09 - 2014.01 Graduate research assistant, Fudan University, Shanghai, China
2014.08 - 2017.12 Postdoctoral research associate, Sanford Burnham Prebys Medical Discovery Institute at Lake Nona, Orlando, FL, USA
2018.01 - present Postdoctoral research fellow, Vanderbilt University Medical Center, Division of Cardiovascular Medicine, Nashville, TN, USA

Memberships in professional societies

2017.10 – present American Diabetes Association

C. Contribution to Science

1. Ph.D. Graduate Career

Critical role of the forkhead transcriptional factor Foxl2 in craniofacial development

Blepharophimosis, ptosis, epicanthus inversus syndrome (BPES) is an autosomal dominant genetic disorder characterized by small palpebral fissures and other craniofacial malformations, often with (type I) but could also present without (type II) premature ovarian failure. While mutations of the forkhead transcription factor *FOXL2* are associated with and may likely be responsible for many BPES cases, how FOXL2 affects craniofacial development remains to be understood. Through a large-scale *piggyBac* (*PB*) insertion mutagenesis, we have identified a mouse mutant carrying a *PB* insertion ~160 kb upstream of the transcription start site (TSS) of *Foxl2*. The insertion reduces, but not eliminates, the expression of *Foxl2*. This mutant, but not its revertant, displays BPES-like conditions such as midface hypoplasia, eyelid abnormalities, and female subfertility. Further analysis indicates that the mutation does not affect the mandible, but causes premature fusion of the premaxilla-maxilla suture, smaller premaxilla, and malformed maxilla during midface development. We further identified an evolutionarily conserved fragment near the insertion site and observed enhancer activity of this element in tissue culture cells. Analyses using DNase I hypersensitivity assay and chromosome conformation capture assay in developing maxillary and periocular tissues suggest that the DNA region near the insertion site likely interacts with *Foxl2* TSS. Therefore, this mutant presents an excellent animal model for mechanistic study of BPES and regulation of *Foxl2*.

a) **Shi F**, Ding S, Zhao S, Han M, Zhuang Y, Xu T, Wu X. A *piggyBac* insertion disrupts *Foxl2* expression that mimics BPES syndrome in mice. Hum Mol Genet. 2014 Jul 15;23(14):3792-800. PubMed PMID: 24565867.

2. Postdoctoral Career

Natriuretic peptide receptor C (NPRC) as an important regulator of energy metabolism in adipose tissue

Almost two decades ago mice with allelic mutations that disrupt the *Nprc* gene were described with the names ‘longjohn’ and ‘strigosus’ because of their extended body length due to delayed bone ossification, and they were noted to have very little body fat. The three natriuretic peptides, ANP, BNP and CNP are all ‘cleared’ from circulation by the product of the Nprc gene – a membrane receptor called NPRC. Separately, in vivo studies in humans suggested that the cardiac natriuretic peptides (NPs), ANP and BNP could increase fatty acid oxidation in muscle as well as lipolysis in adipose tissue. More recently we showed that in human adipocytes ANP and BNP can promote a brown adipocyte ‘signature’ including mitochondrial biogenesis and uncoupled respiration and in vitro studies further suggested a prominent role for NPs in skeletal muscle fatty acid oxidation.

Given this complex phenotype of bone-overgrowth, a paucity of adipose tissue and a candidate pivotal role of skeletal muscle in the metabolic phenotype of *Nprc* null mice, there is a need to genetically assess the contributions of NPRC in the major metabolic tissues, particularly fat and muscle. To unravel the contribution of adipose vs. muscle for NP-stimulated metabolism in vivo, we generated mice with tissue-specific deletion of the NP clearance receptor, *Nprc*, in adipose tissue ($Nprc^{AKO}$) and in skeletal muscle ($Nprc^{MKO}$). Here we show that, similar to Nprc null mice, $Nprc^{AKO}$ mice, but not $Nprc^{MKO}$ mice, are resistant to high fat diet-induced obesity. $Nprc^{AKO}$ mice exhibit increased energy expenditure, improved insulin sensitivity and higher glucose uptake into brown fat. They are also protected from diet-induced hepatic steatosis and visceral fat inflammation. These findings support the conclusion that NPRC in adipose tissue is a critical regulator of energy metabolism, and suggests that inhibiting this receptor may be an important avenue to explore for combatting metabolic disease.

b) Wu Wei*, **Shi F***, Liu D, Wei Wan, Fang H, Collins S. Adipose-specific deletion of *Nprc* protects against diet-induced obesity and insulin resistance. Presented at Keystone Symposium in Obesity and Adipose Tissue Biology Poster Sessions, 2016 February 15-20, Banff, Alberta, Canada. *Equal contribution as co-first authors.

c) Wu Wei*, **Shi F***, Liu D, Ceddia R, Gaffin R, Fang H, Wei Wan, Collins S. Deletion of the natriuretic peptide 'clearance receptor' *Nprc* in adipose, but not muscle, protects against diet-induced obesity and insulin resistance. Sci. Signal. 10: eaam6870. doi: 10.1126/scisignal.aam6870. 2017 Jul 25. *Equal contribution as co-first authors.

d) **Shi F**, Collins S. Second messenger signaling mechanisms of the brown adipocyte thermogenic program: an integrative perspective. Horm Mol Biol Clin Investig. 2017 Sep 26;31(2). doi: 10.1515/hmbci-2017-0062.

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http://www.researcherid.com/rid/O-5078-2018

D. Research Support

Current funding

2018.01.01 - 2020.12.31 1-18-PDF-110 American Diabetes Association Postdoctoral Fellowship Award