BIOGRAPHICAL SKETCH

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NAME: Guo, Shaodong

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

POSITION TITLE: Professor (Tenured)

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Huazhong Agricultural University	B.S.	08/1989	Biochemistry
Peking University	Ph.D.	08/1995	Molecular Biology & Physiology
Institute of Genetics of Chinese Academy of Sciences	Post-doctor	07/1997	Genetics & Developmental Biology
The University of Illinois at Chicago	Post-doctor	07/2001	Physiology & Endocrinology
Harvard University	Post-doctor	12/2006	Medicine & Cardiovascular Biology

A. Personal Statement

The long-term research goal of my laboratory is to investigate the mechanisms of insulin resistance, diabetes mellitus, and associated chronic diseases aiming at therapeutic and dietary interventions. My lab plans to investigate the Foxo1 signaling in control of metabolism, lifespan, and inflammaging-associated metabolism and tissue homeostasis via expression of their target genes in metabolism and immunity. We will measure changes in cell signaling, gene expression, mitochondrial function, and inflammation in mouse tissues of Foxo1 and mutants, providing biochemical and molecular evidence for our fundamental understanding of the mechanisms of Foxo1 signaling in control of lifespan and health-span. I have obtained extensive training, and acquired broad expertise in several research areas, and kept a high motivation necessary to successfully carry in the fields of metabolism and diabetes. As a postdoctoral fellow at the UIC with Dr. Terry G. Unterman, I carried out pioneering work discovering the role of Foxo1 in the regulation of IGFBP1 gene expression in hepatocytes (***JBC*** 1999). After joining the Children's Hospital Boston with Dr. Morris F. White, I expanded my research to mouse models with diabetes to establish key roles of Foxo1 downstream of the insulin receptor substrate 1, and 2 (IRS1, 2) in control of liver glucose metabolism (***Cell Metabolism*** 2008, ***MCB*** 2009, ***Nature Medicine*** 2009). Since I moved to Texas A&M University in 2009, I become an independent PI supported by NIH, American Heart Association, and American Diabetes Association. I have laid the groundwork for the proposed research by developing tissue-specific knockout mice and measures of metabolites and cellular signaling pathways. My lab at Texas A&M has published more than 100 peer-reviewed publications, which have been cited over 10,000 times in google scholars (***Endocrinology*** 2012 & 2019, ***Diabetes*** 2013, 2018, 2019 & 2021, **Diabetologia** 2023; ***Hypertension*** 2014, ***Circulation Heart Failure*** 2015, *JMCC* 2015, *Circulation Research* 2016, ***Nat. Communication*** 2017, 2024; **Aging Cell** 2023). My lab members have received extensive training in a variety of metabolic, molecular, and physiological assays. Currently, my lab research has integrated insulin signaling studies into other hormones such as glucagon and estrogen actions, hepatokines, and small molecules, in collaborating with several outstanding scientists locally and nationally. As a result of my previous experiences, I am aware of the importance of frequent communication with peers joining national-wide conferences in diabetes and cardiovascular research and of constructing a realistic research plan, timeline, and budget. I build research programs logically on my previous work, unraveling novel function of Foxo1 in control

of lifespan and tissue functions during aging, which will advance our understanding of the molecular basis of longevity and Foxo1 in control of metabolism, immunity and health span, and develop new strategies for SASP interventions in control of inflammaging and chronic diseases. In summary, I have demonstrated records of successful and productive research projects in an area of high relevance in the aging and diabetes population, and my expertise and experience have prepared me to lead projects in the field.

The publications below are closely relevant to this proposal:

1. Pan, Q, Gao, M, Kim, D, Ai, W, Yang, W, Jiang, W, Brashear, W, Dai, Y, Li, S, Sun, Y, Qi, Y, **Guo, S** (2024). Hepatocyte FoxO1 deficiency protects from liver fibrosis via reducing inflammation and TGF-β1-mediated HSC activation. ***Cellular and Molecular Gastroenterology and Hepatology*****,** 17 (1):41-58.
2. Yang, W, Kim, D, Jiang, W, Ai, W, Pan, Q, Rahman, S, Cai, J, Brashear, W, Sun, Y, **Guo, S** (2023). Suppression of FOXO1 attenuates inflamm-aging and improves liver function during aging. ***Aging Cell,*** 22 (10) e13968. doi: 10.1111/acel13968.
3. Yang, W, Liao, W, Li, X, Ai, W, Pan, Q, Shen, Z, Jiang, W, **Guo, S** (2023) Hepatic p38α MAPK controls gluconeogenesis via FOXO1 phosphorylation at S273 during glucagon signalling in mice. ***Diabetologia,*** 66(7):1322-1339.
4. Pan, Q, Ai, W, Chen, Y, Kim, D, Shen, Z, Yang, W, Jiang, W, Sun, Y, Safe, S, **Guo, S** (2023) Reciprocal regulation of hepatic TGF-β1 and Foxo1 controls gluconeogenesis and energy expenditure. ***Diabetes,*** db230180. doi.org/10.2337/db23-0180

Ongoing research support:

R01 DK124588
NIH/NIDDK 12/01/2021-11/30/2025
National Institutes of Health/NIDDK
Hepatic TGFbeta1 in Control of Type2 Diabetes Mellitus and NASH via Foxo1 Signaling
This project investigates the role of hepatokine TGFbeta1 in diabetes and liver function of mice.
Role: Principal Investigator (PI)

Texas A&M Advancing Discovery to Market and Innovation Award 8/31/2023-8/31/2025
Novel Discovery of HO1 chemical inhibitor for treatment of Type2 Diabetes and NASH
Role: Principal Investigator (PI)
This project employes high-through-put technology to screen chemical libraries to discover novel chemical inhibitors for heme-oxygenase-1 for prevention diabetes and metabolic inflammation.
Role: Principal Investigator

R01 AG064869 Sun (PI) 5/31/2018-6/31/2024
NIH/NIA
GHS-R in macrophage reprogramming and inflamm-aging
The major goal of this project is to determine how ghrelin receptor regulates immunometabolism and macrophage function in aging of mice.
Role: Co-Investigator

Recently completed projects:

R01 DK120968 5/31/2019-5/31/2023
NIH/NIDDK
Targeting Insulin Resistance by Estrogen Receptor in Control of Type 2 Diabetes
The major goal of this project is to investigate how estrogen receptor enhances insulin sensitivity via interaction of the insulin receptor substrate system
Role: Principal Investigator (PI)

R01 DK-118334 Sun (PI) 6/31/2019-6/31/2023
NIH/NIDDK
The role of GHS-R in macrophage reprogramming during meta-inflammation
The major goal of this project is to investigate how ghrelin receptor regulates insulin sensitivity via macrophage polarization and inflammation.
Role: Co-Investigator

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments:

2022- Pres. Professor, Department of Nutrition, Texas A&M University, College Station, Texas, USA.
2015-2022 Associate Professor (Tenure), Department of Nutrition and Food Science, Texas A&M University, College Station, TX
2015 Associate Professor (Tenure), Department of Medicine and Department of Medical Physiology, Texas A&M University Health Science Center, Temple, TX
2009-2015 Assistant Professor (Tenure-track), Division of Molecular Cardiology, Department of Medicine, Texas A&M University Health Science Center, Temple, TX
2007-2009 Instructor in Medicine at Children's Hospital Boston and Harvard Medical School, Boston, MA
2004-2007 Research Associate in Howard Hughes Medical Institute, Children's Hospital Boston, Harvard Medical School, Harvard University, Boston, MA
2001-2004 Research Fellow in Molecular Medicine and Cardiovascular Biology, Department of Medicine at Beth Israel Deaconess Medical Center and Brigham and Women's Hospital, Harvard Medical School, Harvard University, Boston, MA.
1997-2001 Research Associate in Endocrinology, Department of Medicine, University of Illinois at Chicago.
1995-1997 Research Associate and Principal Investigator, Institute of Genetics and Developmental Biology of Chinese Academy of Sciences, Beijing.

Other Experience and Professional Memberships

2024-2026 Standing member for NIH study section of Diabetes, Endocrinology, and Metabolic Diseases (DDK-B)
2024 Feb. Ad hoc member for NIH study section of Pathophysiology of Obesity and Metabolic Disease (POMD)
2018-2023 Editorial Board Member, *Diabetes,* a scholarly journal of American Diabetes Association
2017-2019 Ad hoc member for NIH study section of Diabetes, Endocrinology and Metabolic Diseases B (DDK-B)
2016-2023 Ad hoc member for NIH study section of Molecular and Cellular Endocrinology (MCE)
2016- Pres. Member, American Nutrition Society
2015 Ad hoc Reviewer of the NIH ZDK1-GRB-7 for SEP section on Metabolic Diseases
2015-2023 Member, Peer Reviewer of American Diabetes Association Study
2014-2020 Member, Peer Reviewer of American Heart Association Study Section Signaling III
2012-2018 Senior Editor, Journal of Molecular Endocrinology
2012-2018 Senior Editor, Journal of Endocrinology
2010- Pres. Member, American Physiology Society
2010- 2015 Member, Graduate Studies of Texas A&M Health Science Center, TX
2003- Pres. Member, Basic Cardiovascular Research Council of American Heart Association
2003- Pres. Member, American Heart Association
2001- Pres. Member, American Diabetes Association
1998-Pres. Member, The Endocrine Society Section

Honors

2023 Texas A&M University Innovation Award, College Station, Texas.
2022 Dean's Outstanding Achievement Award for Research, College of Agriculture and Life Sciences, Texas A&M University, College Station, Texas
2021 Presidential Impact Fellow Award, Texas A&M University, College Station, Texas
2019-2020 Distinguished Reviewer Award for *Diabetes*, scholarly journal of American Diabetes Association
2015-2020 American Diabetes Association Career Development Award
2015 Thomas R. Lee Research Excellence Award from the American Diabetes Association
2007-2010 American Diabetes Association Junior Faculty Award
1999 American 81st Annual Meeting of Endocrine Society Competitive Travel Award, USA
1995-1997 Young Investigator Award, The National Natural Science Foundation of China
1995-1997 Young Investigator Award, Institute of Genetics and developmental Biology of the Chinese Academy of Sciences, Beijing
1992-1995 Winner of Guanghua Scholarship for Outstanding Ph.D. Candidate, Beijing University, China

C. Contributions to Science

My research has led to several mechanism discoveries of how hormonal and nutritional signaling integrate to metabolic regulation in control of glucose and tissue homeostasis and has important impacts on nutritional therapeutic intervention in control of chronic and metabolic diseases. Below are some of my major contributions to the field over the past 20 years.

1. **Transcriptional regulation of gene expression by insulin:** Understanding the molecular mechanism of insulin signaling in control of gene expression is fundamental to decipher insulin resistance, the major underlying mechanism for Type 2 diabetes mellitus and cardiovascular dysfunction. My early publications directly addressed the key signaling molecules responsible for insulin action in control of gene expression and hepatic glucose production. Working with my former mentor Dr. Unterman at UIC, we were the first to establish that forkhead/winged helix transcription factor Foxo1 (known as FKHR) is a critical mediator of insulin signaling downstream from PI3K and Akt in control of expression of many genes, including IGF-binding protein-1 and gluconeogenic enzymes (e.g. glucose-6-phosphatase). The pioneering work was published see below (a), receiving nearly 600 citations so far and followed by many scientists over the world. In addition, we were the first to establish another transcription factor C/EBP that interacts with CREB and CBP/p300 in control of gene expression with Foxo1. I served as the primary investigator or co-investigator in all of these studies.

   a. **Guo S**, Rena G, Cichy S, He X, Cohen P, Unterman T. (1999). Phosphorylation of serine 256 by protein kinase B disrupts transactivation by FKHR and mediates effects of insulin on IGF binding protein-1 promoter activity through a conserved insulin response sequence. ***J. Biol. Chem****.,* 274 (24),17184-17192. PMID:10358076 **[Citations 701]**

   b. **Guo S**, Cichy S, He X, Ghosh AK, Jonson PF, Unterman T. (2001). Insulin suppresses transactivation by CAAT/enhancer-binding protein b(CEBPb): Signaling to p300/CREB binding protein by protein kinase B disrupts interaction with the major activation domain of C/EBPb. ***J. Biol. Chem****.,* 276 (11): 8516-8523. PMID:11116148 **[Citations 103]**

   c. Zhang, K, Li L, Qi Y, Zhu X, Gan B, DePinho R, Averitt T, **Guo S.** (2012). Hepatic Suppression of Foxo1 and Foxo3 Causes Hypoglycemia and Hyperlipidemia in Mice. For editorial preview see page 549-510**.** ***Endocrinology*** 153 (2): 631-646, 2012. PMID: 22147007 **[Citations 204]**

   d. Zhang K, Yan H, Wu Y, Pan Q, Shen Z, Li X, Chen Y, Li L, Qi Y, Xu Z, Xie W, Zhang W, Threadgill D, He L, Villarreal D, Sun Y, White M, Zheng H, **Guo, S** (2019). Phosphorylation of forkhead protein FoxO1 at Ser 253 regulates glucose homeostasis in mice. ***Endocrinology*** 2019, 160 (5): 1333-1347. PMID: 30951171 **[Citations 36]**

2. **Molecular basis of insulin signaling and mitochondrial biogenesis:** With my former mentor Dr. Morris F. White in the Children's Hospital Boston and Harvard Medical School, we established that insulin receptor substrate 1, 2 (IRS1, 2) are key mediators for insulin action in control of not only glucose and lipid metabolism, but also the mitochondrial biogenesis, function, and metabolic information.

   a. **Guo S**, Copps K, Dong X, Park S, Cheng Z, Pocai A, Rossetti L, Sajan M, Farese R, White MF. (2009). Irs1-branch of the insulin signaling cascade plays a dominant role in hepatic nutrient homeostasis. ***Molecular and Cellular Biology****,* 29(18):5070-5083. PMID:19596788 **[Citations 171]**

   b. Cheng Z, **Guo S**, Copps K, Dong X, Kollipara R, Rodgers J, Depinho R, Puigserver P, White MF. (2009). Foxo1 integrates insulin signaling with mitochondrial function in the liver. ***Nature Medicine***, 15(11):1307-1311. PMID:19838201 **[Citations 357]**

   c. Liao W, Yang W, Shen Z, Ai W, Pan Q, Sun Y, **Guo S**. (2021) Heme Oxygenase-1 Regulates Ferrous Iron and Foxo1 in Control of Hepatic Gluconeogenesis. ***Diabetes*** 2021, 70: 696-709. PMID:33408127 **[Citations 25]**

   d. Yang, Y, Jiang, W, Liao, W, Yan, H, Ai, W, Pan, Q, Brashear, WA, Xu, Y, He, L, **Guo S** (2024). An estrogen receptor α-derived peptide improves glucose homeostasis during obesity. ***Nature Communication*** 15, 3410/doi.org/10.1038/s41467-024-47687-6 **[Citations 4]**

3. **Hormonal and nutritional signaling in control of glucose homeostasis, NASH, and aging**: In addition to insulin, other hormones, such as glucagon, estrogen, and ghrelin, also play important roles in control of

glucose and tissue homeostasis. Since I set up my independent lab at Texas A&M, we discovered novel roles of Foxo1 in control of glucose homeostasis in mediating the action of glucagon via protein kinase A (PKA), as well as the action of estrogen via AKT in control of glucose homeostasis and sexual dimorphism, we have important fundament findings in the field enhancing our understanding of disease mechanisms for the therapeutic and nutritional interventions.

a. Wu Y, Pan Q, Yan H, Zhang K, Guo X, Xu Z, Yang W, Qi Y, Guo C, Hornsby C, Zhang L, Zhou A, Li L, Chen Y, Zhang W, Sun Y, Zheng H, Wondisford F, He L, Guo S. (2018). Novel Mechanism of Foxo1 Phosphorylation in Glucagon Signaling in Control of Glucose Homeostasis. ***Diabetes,*** 67(11):2167-2182. PMID:30201683 **[Citations 93]**

b. Yan H, Zhou F, Yang W, Li X, Pan Q, Shen Z, Han G, Newell-Fugate A, Wu C, Majeti R, Xu Y, Tian Y, Allred K, Allred C, Sun Y, **Guo S.** (2019) Estrogen improves insulin sensitivity and suppresses gluconeogenesis via the transcription factor Foxo1. ***Diabetes***, 68:291-304. PMID:30487265 **[Citations 283]**

c. Pan, Q, Gao, M, Kim, D, Ai, W, Yang, W, Jiang, W, Brashear, W, Dai, Y, Li, S, Sun, Y, Qi, Y, **Guo, S** (2024). Hepatocyte FoxO1 deficiency protects from liver fibrosis via reducing inflammation and TGF-β1-mediated HSC activation. ***Cellular and Molecular Gastroenterology and Hepatology*****,** 17 (1):41-58. **[Citations 13**]

d. Yang, W, Kim, D, Jiang, W, Ai, W, Pan, Q, Rahman, S, Cai, J, Brashear, W, Sun, Y, **Guo, S** (2023). Suppression of FOXO1 attenuates inflamm-aging and improves liver function during aging. ***Aging Cell,*** 22 (10) e13968. doi: 10.1111/acel13968. **[Citations 7]**

4. **Diabetes and its complications in cardiovascular failure:** Insulin resistance is major underlying mechanism of metabolic syndrome, type 2 diabetes mellitus and associated cardiovascular dysfunction. My current lab demonstrated that insulin receptor substrate 1, 2 (IRS1, 2) control cardiac metabolism and function, largely involving control of PI3K and Akt signaling that couples Foxo1 inactivation. Therefore, impairing the IRS and Foxo1 signaling following the western diet-induced insulin resistance and type 2 diabetes, promotes cardiac dysfunction and heart failure. Previously working with my former mentor Dr. Victor Dzau in Brigham & Women's Hospital, I have identified a novel angiotensin II receptor AT1-interacting protein- CAML that transmits AT1 signaling to calcium handling through the transcriptional NFAT activation in control of gene expression (*J. Biol. Chem.* 280: 12536, 2005). Recently my lab members demonstrated that Foxo1 stimulates gene expression of angiotensinogen, the precursor of angiotensin II (AngII), thereby promoting blood pressure. Additionally, my lab also has demonstrated that Foxo1 may interface with other transcription factors, such as estrogen receptor, NFκB, and RTEF-1 in regulating gene expression in control of blood glucose, metabolism, and cardiovascular inflammation.

a. Qi Y, Zhu Q, Xu Z, Thomas C, Kumar R, Feng H, Dostal D, White MF, Baker K, **Guo S**. (2013). Myocardial Loss of IRS1 and IRS2 Causes Heart Failure and is Controlled by p38α MAPK During Insulin Resistance. For editorial highlights see page 3646. ***Diabetes****,* 62:3887-3900. PMID:24159000 **[Citations 213]**

b. Yan H, Yang W, Zhou F, Pan Q, Allred K, Allred C, Sun Y, Threadgill D, Dostal D, Tong C, **Guo S**. (2022) Estrogen Protects Cardiac Function and Energy Metabolism in Dilated Cardiomyopathy Induced by Loss of Cardiac IRS1 and IRS2. **Circulation: Heart Failure**, 2022 (10) 1-15. PMID:35579013 **[Citations 22]**

c. Qi, Y, Zhang, K, Xu, Z, Yong, Q, Wu, Y, Kumar, R, Baker, K, Zhu, Q, Chen, S, **Guo, S**. (2014). Novel Mechanism of Blood Pressure Regulation by Foxo1-Mediated Transcriptional Control of Hepatic Angiotensinogen. ***Hypertension****,* 64 (5): 1131-1140. PMID:25069665 **[Citations 35]**

e. Qi, Y, Zhu, Q, Qi, Y, Zhang, K, Thomas, C, Wu, Y, Kumar, R, Baker, K, Xu, Z, Chen, S**, Guo, S**. (2015). Activation of Foxo1 by Insulin Resistance Promotes Cardiac Dysfunction and β-Myosin Heavy Chain Gene Expression. ***Circulation: Heart Failure****,* (8):198-208. PMID:25477432 **[Citations 97]**

Complete List of Published Work in MyBibliography: (151 publications, citations: 10,995; h-factor 45)

http://www.ncbi.nlm.nih.gov/sites/myncbi/shaodong.guo.1/bibliograpahy/46029871/public