

BIOGRAPHICAL SKETCH

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NAME Wenhong Cao		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login)			
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)	MM/YY	FIELD OF STUDY
Hunan Medical University, Hunan, China	M.D.	1978-1983	Medicine
Hunan Medical University, Hunan, China	Residency	1983-1987	Internal Medicine
Hunan Medical University, Hunan, China	M.S.	1987-1990	Hematology
Certified by the U.S. Medical Board (ECFMG) (ID#: 0-553-362-5)		1997	

A. Personal Statement

I have been trying to find new and more effective ways to prevent and treat obesity and diabetes and their associated cardiovascular disorders by investigating mechanisms of obesity, insulin resistance, and type 2 diabetes mellitus (T2DM) for nearly two decades. As an independent investigator, I have made several important discoveries. Results from my lab have first shown that p38 MAPK stimulates hepatic gluconeogenesis while inhibiting hepatic lipogenesis. We have discovered several different ways that can be potentially used to decrease blood glucose level in diabetes by inhibiting hepatic gluconeogenesis via: a) blockade of p38 MAPK; b) application of stromal cell-derived factor-1; c) application of α -defensin, and d) EGCG from tea. In studying mechanisms of insulin resistance, we have found that prolonged exposure to insulin due to positive energy imbalance causes oxidative stress and insulin resistance via inhibition of mitochondrial biogenesis and autophagy-dependent removal of mitochondria. We have also first discovered that increased basal insulin signaling due to positive energy imbalance causes insulin resistance and appropriate blockade of insulin signaling can prevent development of insulin resistance. We have recently observed that p38 may play a critical role in foam cell formation through regulation of autophagy-dependent degradation of cholesterol esters. We are currently investigating mechanisms by which insulin converts the excess calories into insulin resistance, T2DM, and atherosclerosis.

B. Positions and Honors**Positions and Employment**

1990 - 1992 Assistant Professor, Hematology, Hunan Medical University
 1992 - 1993 Associate Professor, Hematology, Hunan Medical University
 1993 - 1998 Research Associate, Duke University Medical Center
 1998 - 2003 Senior Research Associate, Duke University Medical Center
 2003 - 2004 Research Assistant Professor, Duke University Medical Center
 2004 - 2008 Assistant Investigator, The Hamner Institutes for Health Sciences
 2004 - 2008 Assistant Consulting Professor, Duke University Medical Center
 2008 - 2011 Associate Investigator, The Hamner Institutes for Health Sciences
 2008 - present Associate Consulting Professor, Duke University Medical Center
 2011 - present Associate Professor, Department of Nutrition, UNC at Chapel Hill, NC

Other Experience and Professional Memberships

2008 – present American Journal of Physiology: Endocrinology and Metabolism, Editorial Board member
 2009 – present Grant reviewer, American Association (ADA)
 2009 - present Grant reviewer, American Heart Association (AHA)

2009 Grant reviewer, NIH challenge grants
2011 – present BBA-Metabolism and Cell Biology of Lipids , Editorial Board Member
2011 - present Journal of Biological Chemistry, Editorial Board member

Honors

2000 Travel Grant Award for research presentation in “Obesity and Diabetes” session of Endocrine Society Annual Meeting, Toronto, CA
2001 President’s Poster Session Award for research presentation at The American Diabetes Association 61st Scientific Sessions, Philadelphia, PA
2002 Travel Grant Award for research presentation at The American Diabetes Association 62nd Scientific Sessions, San Francisco, CA
2008 Highlighted by American Society for Biochemistry and Molecular Biology (ASBMB) Today (May 2008) on work on defensin suppression of hepatic gluconeogenesis
2009 Star Reviewer Award from American Physiological Society and the American Journal of Physiology: Endocrinology and Metabolism.

C. Selected Peer-reviewed Publications (Selected from 34 peer-reviewed publications)

1. **Cao, W.**, Collins, Q.F., Becker, T.C., Robidoux, J., Lupo, E.G. Jr., Xiong, Y., Daniel, K.W., Floering, L.M., Collins, S. p38 Mitogen-activated protein kinase plays a stimulatory role in hepatic gluconeogenesis. **J. Biol. Chem.**, **2005**, 280:42731-7 (**Note:** Cao was the correspondent)
2. Collins, Q.F., Xiong, Y., Lupo, E.G., Jr., Liu, H.Y., and **Cao, W.** p38 mitogen-activated protein kinase mediates free fatty acid-induced gluconeogenesis in hepatocytes. **J. Biol. Chem.**, **2006**, 281: 24336-44.
3. Xiong, Y., Collins, Q.F., Lupo, E.G., Jie, A., Liu, H.Y., Liu, D.L., Robidoux, J., Pluta, L., and **Cao, W.** p38 MAPK plays an inhibitory role in hepatic lipogenesis. **J. Biol. Chem.**, **2007**, 282:4975-82.
4. Liu, H.Y., Collins, Q.F., Xiong, Y., Fatiha Moukdar, Lupo, E.G. and **Cao, W.** Prolonged treatment of primary hepatocytes with oleate induces insulin resistance through p38 mitogen-activated protein kinase. **J. Biol. Chem.** **2007**, 282: 14205-12.
5. Li, G., Barrett, E.J., **Cao, W.**, Z. Liu. Tumor necrosis factor-alpha induces insulin resistance in endothelial cells via a p38 mitogen-activated protein kinase-dependent pathway. **Endocrinology**, **2007**, 48:3356
6. Collins, Q.F., Liu H.Y., Xiong Y., Quon, M., and **Cao, W.** Epigallocatechin gallate (EGCG) suppresses hepatic gluconeogenesis through AMP activated protein kinase (AMPK). **J. Biol. Chem.**, **2007**, 282:30143-49.
7. Chai, W., Wu, Y., Li, G., **Cao, W.**, Yang, Z., and Liu Z. Activation of p38 mitogen-activated protein kinase abolishes insulin-induced myocardial protection against ischemia-reperfusion injury. **A. J. P.: Endocrinology and Metabolism**, **2008**, 294:E183-94.
8. Kim, J.H., Kim, J.E., Liu, H.Y., **Cao, W.**, and Jie, C. IL-6 induces hepatic insulin resistance through the signaling pathway involving mTOR, STAT3, and SOCS3. **J. Biol. Chem.**, **2008**, 283:708-15
9. Liu, H.Y., Zhuo D., Collins, Q.F., Xiong, Y., Lupo, E.G., and **Cao, W.** Suppression of hepatic gluconeogenesis by Human neutrophil peptides through a novel signaling pathway distinct from insulin. **J. Biol. Chem.**, **2008**, 283: 12056-63.
10. Liu, H.Y., Wen, G.B., Han, J.M., Hong, T., Zhuo, D., Liu, Z., and **Cao, W.** Inhibition of gluconeogenesis in primary hepatocytes by stromal-derived factor-1 (SDF-1) through a c-Src/Akt-dependent signaling pathway. **J. Biol. Chem.**, **2008**, 283: 30642-9.
11. Liu, H.Y., Schnaidman, E.Y., Hong, T., Han, J., Zhuo, D., Liu, Z., **Cao, W.** Prolonged exposure to insulin suppresses mitochondrial production in primary hepatocytes. **J. Biol. Chem.**, **2009**, 284: 14087-95.
12. Li, G, Barrett, EJ, Ko, SH, **Cao, W**, Liu Z. Insulin and IGF-I receptors differentially mediate insulin-stimulated adhesion molecule production by endothelial cells.

Endocrinology, 2009, 150: 3475-82.

13. Liu, H.Y., Hong, T., Han, J., Zhuo, D., Liu, Z., **Cao, W.** Insulin is a stronger inducer of insulin resistance than hyperglycemia in mice with type 1 diabetes mellitus (T1DM).

J. Biol. Chem., 2009, 284: 27090-100.

14. Liu, H.Y., Hong, T., Han, J., Zhuo, D., Liu, Z., **Cao, W.** Increased basal level of Akt-dependent insulin signaling is associated with decreased mitochondrial production and increased ectopic fat accumulation and oxidative stress in the presence of insulin resistance.

AJP: Endocrinology and Metabolism, 2009, 297: E898-08.

15. Liu, H.Y., Han, J.M., Hong, T., Zhuo, D.G., Shi, J.B., Liu, Z., **Cao, W.** Hepatic autophagy is suppressed in the presence of insulin resistance and hyperinsulinemia: inhibition of FoxO1-dependent expression of key autophagy genes by insulin.

J. Biol. Chem., 2009, 284: 31484-92.

16. Wang, N., Ko, S.H., Chai, W., Li, G., Barrett, E.J., Tao, L., **Cao, W.**, and Z. Liu. Resveratrol recruits rat muscle microvasculature via a nitric oxide-dependent mechanism that is blocked by tumor necrosis factor- α .

AJP: Endocrinology and Metabolism, 2010, 300:195-201.

17. Ning, J., Hong, H., Ward, A., Pi, P., Liu, Z., Liu, H.Y., and **Cao, W.** Constitutive role for IRE1 α -XBP1 signaling pathway in the insulin-mediated hepatic lipogenic program.

Endocrinology, 2011, 152: 2255

18. Liu, J., Jahn, L.A., Fowler, D.E., Barrett, E.J., **Cao, W.**, and Z. Liu. Free fatty acids induce insulin resistance in both cardiac and skeletal muscle microvasculature in humans.

J. Clin Endocrin Metab, 2011, 96: 538-46.

19. Hong, T., Liu, H.Y., Liu, Z., and **Cao, W.** Fine-tuned regulation of the PGC-1 α gene transcription by different intracellular signaling pathways.

AJP: Endocrinology and Metabolism, 2011, 300: 500-7.

20. Liu, H.Y., Hong, T., Liu, Z., and **Cao, W.** Insulin and insulin signaling are required for fat induction of insulin resistance in mouse.

AJP: Endocrinology and Metabolism, 2011, accepted on March 15, 2011.

Research Support

Name of funds

Dates of Approved/Proposed Project

Active

1. R01 DK076039-01-A2 (P.I.) 07/01/2007-06/30/2012
NIH/NIDDK
p38 MAPK regulation of hepatic gluconeogenesis and lipogenesis

The main goal of this project is characterize the promoter elements and related transcription factors involved in regulation of the PGC-1 α promoter by p38; define the mechanism by which p38 regulates transcription of the PGC-beta gene; study the key components involved in p38 regulation of the SREBP-1c promoter; and test the hypothesis that blockade of p38 can reduce blood glucose levels in diabetes.

2. Research Grant (P.I.) 07/01/2009-06/30/2012
American Diabetes Association (ADA)
Insulin causes insulin resistance and type 2 diabetes mellitus

The main goal of this project is determine how excessive exposure to insulin induces insulin resistance through inhibition of new mitochondrial production via mitochondrial biogenesis and blockade of removal of old/dysfunctional mitochondria via autophagy in mice with type 1 diabetes.

Pending

1. 1R01DK094928-01 (P.I.) 01/01/2012-12/31/2016
NIH/NIDDK

Title: Regulation of insulin sensitivity and gluconeogenesis by new insulin receptor isoforms

The main goal of this project is characterize the regulatory roles of our newly identified insulin receptor isoforms in hepatic gluconeogenesis and development of insulin resistance.

2. Established Investigator Grant (P.I.) 01/01/2012-12/31/2016
American Heart Association (AHA)

Roles of p38 MAPK and insulin in foam cell formation and stabilization of atherosclerotic plaques.

The main goal of this project is determine the roles of p38 MAPK and insulin signaling in formation and stabilization of atherosclerotic plaques.

Completed

1. Scientist Development Grant (P.I.) 01/01/2005-12/31/2008
(0530244N)

American Heart Association

Regulation of hepatic gluconeogenesis by p38 mitogen-activated protein kinase

The main goal of this project is to determine whether p38 phosphorylation of the PGC-1 α protein is required for hepatic gluconeogenesis; whether CRE/CREB is required for p38 regulation of hepatic gluconeogenesis; and the signaling pathway by which p38 is activated by glucagon in hepatocytes.

2. Measurement of hepatic glucose production (P.I.) 01/01/2007-12/31/2007

GSK

Role of RU486 in hepatic glucose production

The main goal of this project is to determine the role of RU 486 in regulation of hepatic gluconeogenesis of diabetic rats.

3. Measurement of hepatic glucose production (P.I.) 01/01/2008-10/20/2008

AtheroGenics, Inc.

Role of AIG-1067 in hepatic glucose production

The main goal of this project is to determine the role of AIG-1067 in regulation of hepatic gluconeogenesis of diabetic rats.