CURRICULUM VITAE

Haiyan Xu, M.D., Ph.D.

BUSINESS ADDRESS

Hallett Center for Diabetes and Endocrinology Rhode Island Hospital Warren Alpert Medical School of Brown University 55 Claverick St., Rm 318 Providence, RI 02903 Tel. 401-444-0347 Fax. 401-444-3784 Haiyan_Xu@brown.edu hxu@lifespan.org

EDUCATION

Beijing Medical University, Beijing, China	Basic Medicine, M.D., 1992
Beijing Medical University, Beijing, China	Biochemistry, M.S., 1994
Harvard University, Cambridge, MA	Medical Sciences, Ph.D., 2000

POSTGRADUATE TRAINING

Postdoctoral fellow Department of Metabolic Disease Biology Millennium Pharmaceuticals Inc. Cambridge, MA

June 2000 – April 2001

HONORS AND AWARDS

Medical Sigma Xi Harvard-Radcliffe Chapter Scientific Recognition Award	1999
Edgar Haber Award in Biological Sciences by Harvard School of Public Health	2000
Bruce Selya Excellence in Research Award by Rhode Island Hospital	2010
Travel award for NIDDK new PI workshop	2010

ACADEMIC APPOINTMENTS

Assistant Professor of Medicine Warren Alpert Medical School of Brown University Providence, Rhode Island

August 2005 – June 2013

Associate Professor of Medicine

July 2013 - present

OTHER APPOINTMENTS

Research Scientist
Department of Metabolic Disease Biology
Millennium Pharmaceuticals Inc.
Cambridge, MA

April 2001 – October 2003

Associate Research Investigator Metabolic Disease Research Abbott Laboratories Abbott Park, IL

January 2004 – July, 2005

HOSPITAL COMMITTEES

Fellowship research committee for two Pediatric Endocrinology clinical fellows (2009-2011).

UNIVERSITY COMMITTEES

- 1. Admission committee for Pathobiology Program
- 2. Curriculum committee for Pathobiology Program
- 3. Thesis and defense committee for Pathobiology Program MD/PhD student Tecla Temu (2009-2010).
- 4. Thesis and defense committee for PhD student of Boston University, Patricia M. Bedard (2010).
- 5. Thesis committee for Pathobiology Program PhD student Adeola Adebayo (2012-2013).

JOURNAL PEER REVIEW (Ad Hoc)

Biochimica et Biophysica Acta

Cell Death and Differentiation

Diabetes

Endocrine

Endocrinology

FEBS Journal

International Journal of Obesity

Journal of Biological Chemistry

Key Opinions

Medicinal Research Reviews

Molecular and Cellular Endocrinology

Obesity

PLoS ONE

Regulatory peptide

JOURNAL EDITORIAL BOARD

PLoS ONE (Academic editor)

GRANT REVIEW (Ad Hoc)

Diabetes UK 2008

NIH NRSA fellowship review panel Oct. 2010-June 2011

NIH R01 Special Emphasis study section May 2011

NIH IPOD study section Feb. 2012

NIH R15 Special Emphasis Panel ZRG1 EMNR-S Nov 2012

NIH small business grant ZRG1 EMNR-E (10) study section March 2013

NIH small business grant ZRG1 EMNR-S (10) study section Nov. 2013

PROFESSIONAL MEMBERSHIP

The Endocrine Society	1998 - present
The Sigma Xi scientific society Harvard-Radcliffe Chapter	2000 - present
The American Diabetes Association	2005 - present
The American Heart Association	2011 - present

PUBLICATION LIST

ORIGINAL PUBLICATIONS IN PEER_REVIEWED JOURNALS

1. <u>Haiyan Xu</u>, Jaswinder Sethi, Gökhan S. Hotamisligil. The transmembrane form of tumor necrosis factor-α inhibits adipocyte differentiation by selectively activating TNF receptor I. *Journal of Biological Chemistry 274 (37): 26287-26295, 1999*

- **2.** Jaswinder K. Sethi, <u>Haiyan Xu</u>, K. Teoman Uysal, Sarah M. Wiesbrock, Ludger Scheja, and Gökhan S. Hotamisligil. Characterization of receptor-specific TNFα functions in adipocyte cell lines lacking TNF receptors. *FEBS letters* 469: 77-82, 2000
- **3.** Qiang Tong, Gökhan Dalgin, <u>Haiyan Xu</u>, Chao-Nan Ting, Jeffrey M. Leiden, Gökhan S. Hotamisligil. Function of GATA transcription factors in preadipocyte-adipocyte transition. *Science* 290: 134-38, 2000
- **4.** <u>Haiyan Xu</u>, Gökhan S. Hotamisligil. Signaling pathways utilized by tumor necrosis factor receptor 1 in adipocytes to suppress differentiation. *FEBS letters 506: 97-102, 2001*
- **5.** Chiara Chiellini, Anna Bertacca, Silvia E. Novelli, Cem Z. Görgun, Annamaria Ciccarone, Antonio Giordano, <u>Haiyan Xu</u>, Alexander Soukas, Mario Costa, Daniele Gandini, Roberto Dimitri, Pietro Bottone, Paolo Cecchetti, Ennia Pardini, Lucia Perego, Renzo Navalesi, Franco Folli, Luca Benzi, Saverio Cinti, Jeffrey M. Friedman, Gökhan S. Hotamisligil, Margherita Maffei. Obesity modulates the expression of haptoglobin in the white adipose tissue via TNFα. *Journal of Cellular Physiology* 190 (2):251-8, 2002
- **6.** <u>Haiyan Xu</u>, K. Teoman Uysal, J. David Becherer, Peter Arner and Gökhan S. Hotamisligil. Altered TNFα processing in adipocytes and increased expression of transmembrane TNFα in obesity. *Diabetes 51 (6), 1876-1883, 2002*
- **7.** <u>Haiyan Xu</u>, Jiro Hirosumi, K. Teoman Uysal, A. Deniz Guler and Gökhan S. Hotamisligil. Exclusive action of transmembrane TNFα in adipose tissue leads to reduced adipose mass and local but not systemic insulin resistance. *Endocrinology 143 (4): 1502-11, 2002*
- **8.** <u>Haiyan Xu</u> (corresponding author), Marlene Dembski, Qing Yang, Daseng Yang, Ann Moriarty, Olga Tayber, Hong Chen, Rosana Kapeller and Louis A. Tartaglia. Dual specificity MAP kinase phosphatase-4 plays a potential role in insulin resistance. *Journal of Biological Chemistry* 278 (32): 30187-30192, 2003
- **9. Haiyan Xu**, Glenn T. Barnes, Qing Yang, Guo Tan, Daseng Yang, Chieh J. Chou, Jason Sole, Andrew Nichols, Jeffrey S. Ross, Louis A. tartaglia and Hong Chen. Chronic inflammation in adipose tissue plays a crucial role in the development of obesity-related insulin resistance. *Journal of Clinical Investigation*, 112 (12): 1821-1830, 2003 PMCID: PMC296998
- **10.** Suk-Bong Hong, Thomas H. Lubben, Christine M. Dolliver, Anthony J. Petrolonis, Rebecca A. Roy, Zhi Li, Thomas F. Parsons, Ping Li, <u>Haiyan Xu</u>, Regina Reilly, James M. Trevillyan, Andrew J. Nichols, Peter J. Tummino, Thomas G. Gant. Expression, purification, and enzymatic characterization of the dual specificity mitogen-activated protein kinase phosphatase, MKP-4. *Bioorganic Chemistry*, 33(1):34-44, 2005
- **11.** <u>Haiyan Xu</u>, Qing Yang, Minhui Shen, Xueming Huang, Marlene Dembski, Ruth Gimeno, Louis A. Tartaglia, Rosana Kapeller and Zhidan Wu. Dual specificity MAP kinase phosphatase-3 activates PEPCK transcription and increases gluconeogenesis in rat hepatoma cells. *Journal of Biological Chemistry*, 280 (43): 36013-8, 2005

- **12.** <u>Haiyan Xu</u> (corresponding author), Denise Wilcox, Phong Nguyen, Martin Voorbach, Thomas Suhar, Sheryl J.Morgan, W. Frank An, Lin Ge, Jack Green, Zhidan Wu, Ruth Gimeno, Regina Reilly, Peer Jacobson, Christine A. Collins, Katherine Landschulz, Terry Surowy. Hepatic knockdown of mitochondrial glycerol-3-phosphate acyltransferase 1 via RNA interference improves the metabolic profile of *ob/ob* mice. *Biochemical and Biophysical Research Communications*, 349 (1), 439-448, 2006
- **13.** <u>Haiyan Xu</u> (corresponding author), Denise Wilcox, Phong Nguyen, Martin Voorbach, Harriet Smith, Thomas Suhar, Regina Reilly, Peer Jacobson, Christine Collins, Katherine Landschulz, Terry Surowy. Hepatic knockdown of stearoyl-CoA desaturase 1 via RNA interference in obese mice decreases lipid content and changes fatty acid composition. *Frontiers in Bioscience*, *12:3781-3794*, 2007
- **14.** Jing Du, Qiu Chen, Hiroshi Takemori, <u>Haiyan Xu</u>. SIK2 can be activated by deprivation of nutrition and it inhibits lipogenic gene expression in adipocytes. *Obesity*, *16*(3): 531-538, 2008
- **15.** Natalie Moroz, Ming Tong, Lisa Longato, Haiyan Xu, Suzanne M. de la Monte. Limited Alzheimer-Type Neurodegeneration in Experimental Obesity and Type 2 Diabetes Mellitus. *Journal of Alzheimer's Disease*, 15(1): 29-44, 2008
- **16.** Ping Jiao, Qiu Chen, Suketu Shah, Jing Du, Bo Tao, Iphigenia Tzameli, Weiqun Yan, <u>Haiyan Xu</u>. Obesity-related upregulation of monocyte chemotactic factors in adipocytes: involvement of NF-κB and JNK pathways. *Diabetes*, *58:* 104-115, 2009 PMCID: PMC2606857
- **17.** Lascelles E. Lyn-Cook, Margot Lawton, Ming Tong, E Silbermann, Lisa Longato, Ping Jiao, P Mark, Jack R. Wands, <u>Haiyan Xu</u>, Suzanne M. de la Monte. Hepatic ceramide may mediate brain insulin resistance and neurodegeneration in type 2 diabetes and non-alcoholic steatohepatitis. *Journal of Alzheimer's Disease*, *16*(*4*): 715-29, 2009 PMCID: PMC2893047
- **18.** Zhidan Wu, Ping Jiao, Xueming Huang, Bin Feng, Yajun Feng, Shengyong Yang, Philip Hwang, Jing Du, Yaohui Nie, Guozhi Xiao, <u>Haiyan Xu</u>. MAP kinase phosphatase 3 promotes hepatic gluconeogenesis through dephosphorylation of forkhead box O1 in mice. *Journal of Clinical Investigation*, 120 (11): 3901-3911, 2010
- **19.** Ping Jiao, Jie Ma, Bin Feng, Hao Zhang, J. Alan Diehl, Y. Eugene Chin, Weiqun Yan, <u>Haiyan Xu</u>. FFA-induced adipocyte inflammation and insulin resistance: involvement of ER Stress and IKKβ pathways. *Obesity*, *19*(*3*):*483-491*, *2011*
- **20**. Shengyong Yang, <u>Haiyan Xu</u>, Shibing Yu, Huiling Cao, Jie Fan, Chunxi Ge, Renny T. Fransceschi, Henry H Dong, Guozhi Xiao. FOXO1 mediates IGF1/Insulin regulation of osteocalcin expression by antagonizing Runx2 in osteoblasts. *Journal of Biological Chemistry*, 286(21):19149-58, 2011

- **21.** Bin Feng, Ping Jiao, Yaohui Nie, Thomas Kim, Dale Jun, Nico van Rooijen, Zaiqing Yang, **Haiyan Xu**. Clodronate liposomes improve metabolic profile and reduce visceral adipose macrophage content in diet-induced obese mice. *PLoS One*, 6(9): e24358, 1-11, 2011
- **22.** Ping Jiao, Bin Feng, Jie Ma, Yaohui Nie, Erin Paul, Yujie Li, <u>Haiyan Xu</u>. Constitutive activation of IKKβ in adipose tissue prevents diet-induced obesity. *Endocrinology*, *153*(1):154-65, 2012
- **23.** Yaohui Nie, Ronald C. Ma, Juliana CN Chan, <u>Haiyan Xu</u> and Gang Xu. Glucose-dependent insulinotropic peptide impairs insulin signaling via inducing inflammation in glucose-dependent insulinotropic peptide receptor over-expressing adipocytes. *FASEB Journal*, 26 (6): 2383-2393, 2012
- **24.** Bin Feng, Ping Jiao, Zaiqing Yang, <u>Haiyan Xu</u>. MEK/ERK pathway mediates insulin-promoted MKP-3 protein degradation in liver cells. *Molecular and Cellular Endocrinology*, *361:116-123*, *2012* PMID:22521266
- **25.** Ping Jiao, Bin Feng, <u>Haiyan Xu</u>. Mapping MKP-3/FOXO1 interaction and evaluating the effect on gluconeogenesis. *PLoS One*, *7*(7): *e41168*, *1-10*, *2012* PMID: 22848439
- **26.** Ping Jiao, Bin Feng, Yujie Li, <u>Haiyan Xu</u>. Hepatic ERK activity plays a role in energy metabolism. *Molecular and Cellular Endocrinology*, 375: 157-166, 2013 PMID: 23732116
- **27.** Yujie Li, Yaohui Nie, Ynes Helou, Bin Feng, Guoxian Ding, Gang Xu, Arthur Salomon, <u>Haiyan Xu</u>. Identification of sucrose non-fermenting related kinase (SNRK) as a suppressor of adipocyte inflammation. *Diabetes*, 62:2396-2409, 2013 PMID: 23520131
- **28.** Otilia Neacsu, Kelly Cleveland, <u>Haiyan Xu</u>, Tamara T. Tchkonia, James L Kirkland, Charlotte M Boney. IGF-I attenuates FFA-induced activation of JNK1 phosphorylation and TNFα expression in human subcutaneous preadipocytes. *Obesity*, *21* (9): 1843-9, 2013 PMID: 23512893

OTHER PEER-REVIEWED PUBLICATIONS

- **1.** Ping Jiao, <u>Haiyan Xu.</u> Adipose inflammation: cause or consequence of obesity-related insulin resistance? Review. *Diabetes, Metabolic Syndrome and Obesity, 1: 25-31, 2008*
- **2.** Bin Feng, Tracy Zhang, <u>Haiyan Xu</u>. Human adipose tissue dynamics and metabolic health. Review. *Annals of the New York Academy of Sciences*, *1281*: *160-177*, *2013*
- **3.** <u>Haiyan Xu</u>. Obesity and metabolic inflammation. Review. *Drug Discovery Today: Disease Mechanism*, 10: e21-e25, 2013

PUBLICATIONS SUBMITTED OR IN PREPARATION

1. Wenliang Zhang, Emilio P Mottillo, Krishna R. Maddipati; Allison Gartung; Jen-Fu Lee; Hiba Jawadi; Jiawei Zhao; <u>Haiyan Xu</u>; Kenneth V. Honn; James G. Granneman, Menq-Jer Lee.

Adipocyte Lipolysis Activates Interleukin 6 Production via Sphingosine-1-phosphate Autocrine Signaling. *Manuscript submitted*

- 2. Bin Feng¹, Ping Jiao^{1,2}, Ynes Helou³, Qin He¹, Matthew Walters⁴, Arthur Salomon^{5,6}, <u>Haiyan Xu</u>^{1,7*} MAP kinase phosphatase 3 (MKP-3) deficient mice are resistant to diet inducedobesity. *Manuscript under revision*
- 3. Bin Feng, Qin He, <u>Haiyan Xu</u>. FOXO1-dependent up-regulation of MAP kinase phosphatase 3 (MKP-3) mediates glucocorticoid-induced hepatic lipid accumulation in mice. *Manuscript submitted*
- 4. Jeffrey W. Hofmann, Xiaoai Zhao, Marco De Cecco, Abigail L. Peterson, Jayameenakshi Manivannan, Yuji Ikeno, Yongqing Zhang, Bin Feng, Wenbo Qi, Holly Van Remmen, Richard A. Miller, Rafael de Cabo, <u>Haiyan Xu</u>, Nicola Neretti and John M. Sedivy. Reduced expression of the proto-oncogene *Myc* increases mouse longevity and enhances healthspan. *Manuscript in preparation*

ABSTRACTS

- 1. <u>Haiyan Xu</u>, K. Teoman Uysal, A. Deniz Guler and Gokhan S. Hotamisligil. Exclusive action of transmembrane TNFα in adipose tissue leads to reduced adipose mass and local but not systemic insulin resistance. Keystone Symposia Meeting Abstract Book, Jan., 2000
- 2. <u>Haiyan Xu</u>, Denise Wilcox, Phong Nguyen, Martin Voorbach, Thomas Suhar, Sheryl J.Morgan, W. Frank An, Lin Ge, Jack Green, Zhidan Wu, Ruth Gimeno, Regina Reilly, Peer Jacobson, Christine A. Collins, Katherine Landschulz, Terry Surowy. Hepatic knockdown of mitochondrial glycerol-3-phosphate acyltransferase 1 via RNA interference improves the metabolic profile of *ob/ob* mice. American Diabetes Association Annual Scientific Session Abstract book, June 2005.
- 3. <u>Haiyan Xu</u>, Denise Wilcox, Phong Nguyen, Martin Voorbach, Harriet Smith, Thomas Suhar, Regina Reilly, Peer Jacobson, Christine Collins, Katherine Landschulz, Terry Surowy. Hepatic knockdown of stearoyl-CoA desaturase 1 via RNA interference in obese mice decreases lipid content and changes fatty acid composition. American Diabetes Association Annual Scientific Session Late Breaking Abstract, 2005.
- 4. Ping Jiao, Weiqun Yan, <u>Haiyan Xu</u>. Role of endoplasmic reticulum stress in free fatty acid-induced insulin resistance in adipocytes: involvement of IKKβ pathway. Keystone Symposia Meeting Abstract Book, Jan., 2010, p83. Dr. Jiao obtained a travel award for this meeting.
- 5. Ping Jiao, Bin Feng, Phillip Hwang, Jing Du, Guozhi Xiao, <u>Haiyan Xu</u>. MAP kinase phosphatase 3 regulates glucose homeostasis through dephosphorylation of FOXO1. The 11th International Congress on Obesity Abstract Book, July 2010, P37.
- 6. Ping Jiao, Bin Feng, Xueming Huang, Yajun Feng, Shengyong Yang, Phillip Hwang, Jing Du, Yaohui Nie, Guozhi Xiao, Zhidan Wu, **Haiyan Xu**. MAP kinase phosphatase 3 regulates glucose homeostasis through dephosphorylation of FOXO1. NIDDK New PI Workshop Abstract Book, Nov. 2010, p3.

- 7. Bin Feng, Ping Jiao, Yaohui Nie, Thomas Kim, Dale Jun, <u>Haiyan Xu</u>. Clodronate liposomes improve metabolic profile and reduce visceral adipose macrophage content in diet-induced obese mice. Endocrine Society Annual Meeting Abstract Book, June 2011, P3-393, page 182
- 8. Ping Jiao, Bin Feng, Jie Ma, Yaohui Nie, <u>Haiyan Xu</u>. Constitutive activation of IKKβ in adipose tissue prevents diet-induced obesity. Endocrine Society Annual Meeting Abstract Book, June 2011, P3-386, page 182
- 9. Bin Feng, Ping Jiao, Yujie Li, Haiyan Xu. MKP-3/DUSP6 promotes lipogenesis. Keystone Symposia Adipose Tissue Biology Meeting Abstract Book, Jan., 2013, page 79
- 10. Yujie Li, Yaohui Nie, Ynes Helou, Guoxian Ding, Gang Xu, Arthur Salomon, Haiyan Xu. Keystone Symposia Adipose Tissue Biology Meeting Abstract Book, Jan., 2013, page 112

INVITED PRESENTATIONS

1. "Obesity and type 2 diabetes: understanding the molecular mechanism" Brown Medical School, Division of Endocrinology Providence, RI

March 18, 2004

2. "Adipose inflammation and obesity-related insulin resistance"

Harvard School of Public Health Nutrition Seminar Series

Boston, MA April 19, 2004

3. "Molecular mechanism of obesity-related type 2 diabetes"

Liver Research Center, Brown Medical School

Providence, RI March 2, 2006

4. "Adipose inflammation and obesity-related type 2 diabetes"

Pediatric Endocrinology, Hasbro Children's Hospital

Providence, RI December 1, 2006

5. "Infiltration of Adipose Tissue by Immune Cells in Obesity: Chicken or Egg?"

9th Postgraduate Nutrition Symposium, Harvard Medical School

Boston, MA March 21-22, 2007

6. "Obesity and adipose inflammation: role of infiltrated macrophages"

Luzhou Medical College, Luzhou, China October 15, 2007

7. "Obesity and adipose inflammation: role of infiltrated macrophages"

October 19, 2007

8. "Obesity and adipose inflammation: role of infiltrated macrophages" Peking University, Health Science Center, Beijing, China

October 22, 2007

9. "Adipose inflammation and obesity"

AGA Institute at Digestive Disease Week 2008, San Diego, CA

May 20, 2008

10. "Adipose inflammation, cause or consequence of obesity-related insulin resistance"

Ortho-Clinical Diagnostics, Inc., a Johnson & Johnson company, Raritan, NJ

Feb. 11, 2010

11. "MAP Kinase Phosphatase 3 Regulates Glucose Homeostasis through Dephosphorylation of FOXO1"

The 11th International Congress on Obesity, Stockholm, Sweden

July 13, 2010

12. "Adipose inflammation and obesity-related insulin resistance"

Boston University, School of Medicine, Boston, MA

Nov.3, 2010

13. "Adipose inflammation and obesity-related insulin resistance"

University of Rhode Island, Kingston, RI

Feb. 3, 2011

14. "Obesity and type 2 diabetes: understanding the molecular mechanism"

Keynote speaker of Lifespan 19th Annual Research Celebration, Providence, RI

Oct. 27, 2011

15. "Obesity and type 2 diabetes: understanding the molecular mechanism"

University of Iowa, Iowa City, IA

April 10, 2012

GRANTS

Active

- **1.** Principal Investigator, 5 R01 DK080746, NIH/NIDDK "MAP kinase phosphatase 3 and obesity-related gluconeogenesis". 1/15/2009 to 11/30/2014, total direct cost, \$1,080,000; total cost, \$1,587,005.
- **2.** Mentor, George A. Bray Research Scholars Award, Brown University (recipient, Dr. Bin Feng), 9/1/2013 to 8/31/2015. Total direct cost, \$70,000.

Pending

- 1. Principal Investigator, American Heart Association grant-in-aid, "SNRK and Adipose Inflammation". 7/1/14 to 6/30/17
- 2. Principal Investigator, NIH/NIDDK, "SNRK and Adipose Energy Homeostasis", 1/1/15 to 12/31/19

Complete

- 1. Principal Investigator, American Heart Association Scientist Development Grant. "Mechanism and consequence of obesity-related adipose macrophage infiltration". 1/1/2008 to 6/30/2012, total direct cost, \$280,000; total cost, \$308,000.
- 2. Principal Investigator: 3 R01 DK080746-02S1, NIH/NIDDK "MAP kinase phosphatase 3 and obesity-related gluconeogenesis" (equipment supplement). 1/8/2010 to 3/31/2010, total direct cost, \$100,000
- 3. Mentor, George A Bray Research Scholars Award, Brown University (recipient, Dr. Ping Jiao), 2/1/2009 to 1/30/2011. Total direct cost, \$30,000.
- 4. Principal Investigator: Charles H. Hood Foundation Child Health Research Grant "The mechanism of MAP kinase phosphatase 3 (MKP-3) induced gluconeogenesis in obesity and diabetes".

1/1/2006 to 12/31/2007, total direct cost, \$136,264; total cost, \$150,000.

- 5. Principal Investigator: The Rhode Island Foundation Medical Research Grant "The function of salt inducible kinase 2 (SIK2) in adipocyte energy metabolism". 1/1/2006 to 12/31/2006, total direct cost \$10,000
- 6. Principal Investigator: Lifespan Developmental Grant "Role of mitogen activated dual specificity kinase phosphatase 3 (MKP-3) in obesity and diabetes related gluconeogenesis". 1/1/2006 to 12/31/2006, total direct cost \$30,000

UNIVERSITY TEACHING ROLES

- 1. Bio2850 for graduate students in pathophysiology program at Brown University
- 2. Bio 195/196 for undergraduate students in Biochemistry and Molecular Biology program at Brown University