Mi-Jeong Lee, PhD

Office Address: Dept of Human Nutrition, Food and Animal Sciences
College of Tropical Agriculture and Human Resources
The University of Hawaii at Manoa
1955 East-West Rd. 314K
Honolulu, HI 96822

Phone: 808-956-9565 (office)

Emails: leemj7@hawaii.edu ; lee.mijeong@gmail.com

ORCID: https://orcid.org/0000-0002-8171-791

Research Gate: https://www.researchgate.net/profile/Mi-Jeong_Lee

EDUCATION:

May 2005 **PhD in Nutritional Biochemistry**
Rutgers, the State University of New Jersey, Department of Nutritional Sciences, New Jersey, USA
Dissertation title: Hormonal and Nutritional Regulation of Leptin Production: Importance of 3' Untranslated Regions

Feb. 1997 **MS in Nutritional Sciences**
Seoul National University, Department of Agricultural Home Economics, College of Agriculture and Life Sciences, Republic of Korea
Dissertation title: Effects of protein intake on the growth and protein metabolism in early weaned rats

Feb. 1995 **BS in Agricultural Home Economics**
Seoul National University, Department of Agricultural Home Economics, College of Agriculture and Life Sciences, Republic of Korea

POSTDOCTORAL TRAINING:

May 2005 – Dec. 2008: Postdoctoral Fellow, Division of Endocrinology, Diabetes and Nutrition, University of Maryland School of Medicine, Baltimore, MD, USA

ACADEMIC APPOINTMENTS:

Oct. 2019: Assistant Professor, Dept. of Human Nutrition, Food and Animal Sciences, CTAHR, The University of Hawaii at Manoa, Honolulu, HI, USA

Oct. 2016-Sept. 2019: Assistant Professor, Dept. of Medicine, Division of Endocrinology, Diabetes, Obesity and Metabolism Institute, Icahn School of Medicine at Mt. Sinai Hospitals, New York, NY, USA

Feb. 2015 – Sept. 2016: Assistant Professor, Dept. of Medicine, Section of Endocrinology Diabetes and Nutrition, Boston University School of Medicine, Boston, MA, USA

Feb. 2014 – Sept. 2016: Assistant Core Director for the Adipocyte Biology and Nutrient Metabolism Core, Boston Nutrition and Obesity Research Center, Boston, MA, USA

Jan. 2009 – Jan. 2015: Instructor, Boston University School of Medicine, Section of Endocrinology, Diabetes and Nutrition, Boston, MA, USA.

ACADEMIC AND PROFESSIONAL HONORS:

2016: *Travel Award,* NIH workshop on The Adipose Tissue Niche: Role in Health and Diseases, NIH, Bethesda, MD, USA

2015: *Travel Award*, Danish Diabetes Research Council meeting, Malaga, Spain

2012: *Faculty Development & Diversity grant*, Boston University School of Medicine, MA, USA

2007-2008: *Post-doctoral Fellowship*, American Heart Association, USA

2003: *Travel Award*, Summer FASEB conference on Obesity, Augusta, GA, USA

2000-2001: *Excellence Graduate Student Fellowship*, Rutgers University, NJ, USA

1995-1997: *Graduate Scholarship,* Seoul National University, Korea

1991-1995: *Scholarship for undergraduate study*, Seoul National University, Korea

OTHER PROFESSIONAL ACTIVITIES:

Manuscripts Peer Reviewer

Diabetes, Journal of Biological Chemistry, International Journal of Obesity, Am J Physiol Endocrinol Metab, Endocrinology, Molecular Metabolism, Journal of Lipid Research, Journal of Nutrition, Journal of Nutritional Biochemistry, Scientific Reports, BBA - Molecular and Cell Biology of Lipids, BBA - General Subjects, PLoS One, Obesity, Biochemical and Biophysical Research Communications, Molecular and Cellular Biochemistry, Nutrition Research and Practice, Functional Foods in Health and Disease, Nutrients, Annual Review of .

Editorial Board Member

Nutrition Research and Practice (2017- current)

National Service

Ad hoc member, AHA-Study Section, Lipids Basic Science, Oct 2013 - April 2016

Other Agencies – *reviewing activities*

Reviewer – P&F grants, Boston Nutrition and Obesity Research Center, Boston University, 2013-2016.
P & F grants for Michigan Diabetes Research Center, 2019 -

Local Activities

2015-2016: Committee member of the Graduate Program in Life Science, BUSM

2014-2016: Member of Admission Committee of the Graduate Program in Nutrition and Metabolism, BUSM

2016-2019: Committee member of the Graduate Program in Biomedical Sciences at Mt. Sinai Medical School

2019-current: Committee member, Nutritional Science Graduate Program in the Dept of Human Nutrition, Food and Animal Sciences at the University of Hawaii at Manoa

Professional Societies

THE OBESITY SOCIETY:

Session Chair, The Obesity Society's 28th Annual Scientific Meeting, 2010.

Professional Society member

2017~ present: American Diabetes Association
2012~ present: American Society for Nutrition
2012~present: The Obesity Society

RESEARCH SUPPORT

Start-up Fund from CTAHR/OVCR University of Hawaii (Lee) 10/01/19-10/31/21
This provide funding to set-up research projects at the University of Hawaii.

Texas Tech University, "Come n' Go" Domestic Research Collaboration Seed Grant, (Latha) 11/01/19-10/31/20
This provide funding for COHS faculty and a collaborator from another US Institution, to visit each other's campuses and to design a collaborative research project. We will study "Role of Fish Oil in Paternal Obesity".
Role: Co-I

NY Diabetes Research Center P& F Grant, 06/01/18-05/31/19, $35,000
"Role of TGFbeta signaling in adipose tissue biology": This study addresses the importance of TGFβ signaling pathway in adipose tissue development and function.
Role: PI

1R01DK080448 (PI: Fried) 07/01/2014-09/30/19
"Glucocorticoids & adipocyte function in human obesity": The goal of this project is to understand how glucocorticoids differentially regulate adipose tissue function in visceral vs. subcutaneous adipose tissue using both in vivo and in vitro approaches.
Role: Co-I

ADA 7-14-BS-059 (PI: Fried) 10/01/14-9/31/17
"Reprogramming Fatty Acid Handling to Improve Adipocyte Function in Human Obesity": The objective of this proposal is to understand how alterations in fatty acid handling, focusing on FABP3 and PLIN5, contribute to a 'brown phenotype' in human adipocytes.
Role: Co-I

P30 DK046200NIH/NIDDK (PI: Fried) 07/01/13-09/30/16
"Boston Nutrition and Obesity Research Center": The purpose of the Adipocyte Core is to provide euploid rodent and human undifferentiated and differentiated mass-cultured and cloned preadipocytes and freshly-isolated and cultured fat cells and products derived from these cells (RNA, DNA, protein, conditioned medium) to BNORC investigators.
Role: Co-I/Assistant Director for the Adipose Biology and Nutrient Metabolism Core

Joslin Diabetes Research Center/BUSM P & F Grant, 03/01/13-6/31/15, $35,000 per year
"Defining the phenotype of brite human adipocytes – a systems biology approach": The goal is to elucidate pathways/networks that lead to the metabolic and endocrine differences between white and brite cells using a systems biology approach, combining transcriptome and metabolomics data.
Role: PI

BU CTSI Microarray Core, internal funding, 4/1/2014-3/31/2015, $2,400
"Glucocorticoid and TNF regulation of adipocyte transcriptome": The goal of this proposal is to identify gene networks that are affected by glucocorticoids and TNF interactions and elucidate the molecular mechanisms by which TNF modulates glucocorticoid action in adipocyte function.
Role: PI

NIH RO1DK101711-01 (PI: Puri) 10/1/14-8/31/15
"Cidea Proteins and Regulation of Energy Expenditure": The major the goal of this project is to identify the molecular mechanisms associated in maintaining 'white' and 'brite' phenotype of human adipocytes, with consequences for the regulation of energy expenditure and FA-induced insulin resistance in obesity and type 2-diabetes.

Role: Co-I

BU Undergraduate Research Opportunity Program (Lesman) 06/01/13-05/31/15
UROP provides research stipends and travel awards to undergraduate students at BU.
Role: Sponsor

1R01DK080448-04 NIH/NIDDK (PI: Fried) 06/01/2009 – 03/31/2014
"Glucocorticoids & adipocyte function in human obesity": The goal of this project is to understand how glucocorticoids promote the development of obesity, and particularly visceral obesity, and its metabolic complications.

Boston University Integrated Biomedical Pilot & Feasibility Grant, 07/01/12-6/30/13, $12,000
"Depot-differences in adipocyte progenitors": The goal is to isolate and characterize different adipogenic precursors from human adipose tissue and compare their relative abundance and characteristics between visceral and subcutaneous adipose depots.
Role: PI

R56DK094815-01A1 NIH/NIDDK (PI: Puri) 09/14/2012 – 08/31/2013
"Role of FSP27 in lipid droplet dynamics": This proposal addresses the role of fat specific protein 27 (FSP27), a lipid droplet protein, in lipid droplet dynamics, lipid droplet fragmentation and enlargement.
Role: Co-I

NIH RO1 DK052398 (PI: Fried) 07/01/07-06/30/12
"Regulation of leptin expression in human adipose tissue": This grant studies the hormonal and nutritional regulation of leptin production from adipocytes using both in vivo animal models and human adipose tissue explants and adipocyte culture models.
Co-I

Interdisciplinary Studies In Sex-differences (ISIS) Network, Studies for Women's Health Research 07/01/10-06/30/11, Direct cost: $10,000
"A survey of miRNAs in adipose tissue across sex and depots"**:** The goal of this project is to survey of miRNAs in adipose tissue across sex and depot will identify one or more novel miRNAs that are important to sex differences in fat mass and distribution. miRNA data are combined with clinical data (demographics) from the ISIS project and the transcriptome analyses.
Role: PI

Pilot and Feasibility Grant from CNRU of Maryland, 1/2008-12/2008, Direct Cost: $14,800
"Role of the Glucocorticoid Receptor in Adipocyte Biology": The goal of this project is to understand the role of glucocorticoid receptor in adipocyte metabolism and endocrine function using human adipose tissue explants and adipocyte culture system.
Role: PI

AHA Post-doctoral fellowship, 7/2007-12/2008, $35,000 per year
"TNFα regulation of glucocorticoid receptor in human adipose tissue": This project studies how TNFα, a proinflammatory cytokine that is more abundantly expressed in obese compared lean and visceral compared to subcutaneous adipose tissue modulates glucocorticoid receptor function in adipose tissue.
Role: PI

TEACHING

I have always enjoyed interactions with students and the main reason that I decided to pursue my career in academia was that I have the opportunity to work with next generation of scientists while continuing my independent research. I believe learning is an active process through which students acquire basic knowledge but also become independent thinkers and as a teacher and mentor, I facilitate the learning process by guiding, stimulating and challenging the students. I also believe that all individuals have his or her own strengths and weaknesses, but it is our responsibility to find out each student's unique strengths and encourage them to develop their own great qualifications but also support them to overcome their weaknesses.

I have continuously developed my teaching skills and have taught students from diverse backgrounds both in Korea and USA as listed below. With my education and teaching experiences at multiple academic institutes, I am confident at teaching students in both seated classroom and on-line. I will create a classroom environment in which students from all backgrounds can reach their potential and learn to think as independent scientists.

- Worked as a Department Office Assistant in the Department of Agricultural Home Economics, Seoul National University, 1997-1998; assisted teaching undergraduate courses, "Nutritional Physiology", "Food and Experimental Cookery", "Nutrition", "Food Preparation".
- Part-time Lecturer, Korean National Open University, in class lecture for "Nutrition throughout the Life Cycle" course, 1998-1999.
- Teaching Assistant for "Nutrition/Biochemistry and Physiology", Rutgers University, 2001-2002, weekly 1h recitation in class room setting and tutoring on need base. Assist journal discussion for the Nutritional Science Seminar.
- Teaching (tutoring and journal discussion), Metabolism Section in Graduate Program in Life Sciences Core Class, "Metabolism", University of Maryland 2007-2008.
- Instructor/Assistant Professor, Boston University 2010-2016 in NU 756: "Molecular, Biochemical and Physiological Bases of Nutrition: Macronutrient Metabolism", lecture and paper discussion "Long term regulation of nutrient absorption and metabolism: Molecular mechanisms". "Nutrition Sciences Seminar", guide students to present their research work. In the latter cases, I initiated those requests to increase diversity and improve my teaching portfolio. I also contributed to developments of nutritional sciences courses along with program directors, Drs. Lynn Moore and Susan Fried.
- Assistant Professor, Icahn School of Medicine at Mount Sinai Hospitals 2016 – 2019: lecture and paper discussion, "Metabolism".
- Assistant Professor, Department of Human Nutrition, Food and Animal Sciences University of Hawaii at Monoa; Nutritional Biochemistry I & II (400 level), Nutrition and Disease: Cellular and Molecular Aspects (600 level), Obesity (400 level), Seminar in Nutritional Science (600 level)

MENTORING AND TRAINING:

I have been mentoring many students and fellows and I am confident in training and mentoring students to achieve their research qualifications. I will actively recruit and mentor students, especially from underrepresented groups, for their graduate research projects and serve as a committee member. Furthermore, I will participate in the university outreach programs and foster women and underrepresented minority undergraduate students to engage in science through summer research program or undergraduate research programs.

- Mentor, Sam Woodle (High school summer student, currently in Military Medical School), University of Maryland, School of Medicine, 2004.
- Mentor, Samuel Antwi (Undergraduate summer student, Howard University), University of Maryland, School of Medicine, 2005.
- Train and mentor, Jamie Fleenor (a research associate, currently working as a research associate at the Johns Hopkins), University of Maryland, School of Medicine, 2003-2004.
- Train and mentor, Ling Duan (a research associate, currently working as a research associate at the University of Pennsylvania), 2003-2005.
- Train Sara Fletcher (Graduate student at University of Tennessee) for 3 mon in adipose tissue organ culture and molecular biology for her MS thesis project, "Regulation of Angiotensinogen production from omental and subcutaneous human adipose tissue", University of Maryland, School of Medicine, summer 2006.
- Train and co-mentor, Urmila Sreenivasan, MS (currently, working as a research associate in School of Medicine University of Maryland), University of Maryland, School of Medicine, 2006-2008.
- Mentor, Vicky Zhang (high school summer student, currently working as a research associate III at Teva Pharmaceuticals), University of Maryland School of Medicine, 2007-2008.
- Train and co-mentor Silvia de Barros-Mazon (currently, associate professor at University of Sao Paulo, Brazil), University of Maryland School of Medicine, 2007-2008.
- Train and co-mentor Christina Dani a MS student at University of Maryland School of Medicine, 2008.
- Train Xia Tao (graduate student at University of Massachusetts) for adipocyte biology, Boston University, summer 2009.
- Train and co-mentor, Weimin Guo, PhD, a postdoctoral fellow (BUSM), 2009-2013. He is currently working as a research fellow at Brigham Women's Hospital.
- Mentor, Kirstin Carswell, M.D., Visiting Scholar from Kings College (BUSM), United Kingdom, 2010 (methods for adipocyte culture). After training in our laboratory, we published a method paper in *Methods Mol Biol*, "Culture of isolated human adipocytes and isolated adipose tissue". She is an Assistant Professor at King's College Hospital, England.
- Train and co-mentor a visiting scholar, Dr. H. Nimitphong, with Dr. Michael Holick (BUMC), 2010-2013. Her research projects was published a paper in *PLoS-One*, "25-hydroxyvitamin D_3 and 1,25-dihydroxy vitamin D_3 promote the differentiation of human subcutaneous preadipocytes" where she assumed the first authorship and I was the corresponding author. Currently, we are preparing to submit another paper. She is an Assistant Professor at Mahidol Hospital, Thailand.
- Co-mentor, Mara Banks, MD/PhD student (BUMC) with Dr. Michael Holick. Currently, she is currently working as a resident at Georgia Hospitals.
- Train and mentor, a BU undergraduate student, Felicia Lesman, 2013~2015. To support her research, we applied for the Undergraduate Research Opportunity Program at Boston University and she was successfully funded for 2 years. Furthermore, she presented her research in the annual meeting of The Obesity Society, 2014: "Thiazolidinediones induction of brite phenotype in subcutaneous human adipose tissue". Currently, she is working as a Medical Assistant at Harvard Vanguard Medical Associates - Atrius Health.
- Mentor, a visiting PhD student, Pia Villarroel from University de Chile, 2014 (BUSM). She

presented her work, "Calcium sensing receptor activation in human subcutaneous adipose depots" for the annual meeting of The Obesity Society, 2014. Her poster presentation was selected as a travel award.

- Co-mentor, Yuanyan Wu, a post-doctoral fellow with Dr. Susan K. Fried (BUMC), 2011-2014, currently working as a research scientist at Pfizer Pharmaceutical. Her work, "High-fat diet-induced obesity regulates MMP3 to modulate depot- and sex-dependent adipose expansion in C57BL/6J mice" in *Am J Physiol Endocrinol Metab*.
- Co-mentor, Stephaine Knebusch Toriello, MS in Molecular Medicine (BUSM), 2014-2015: mentored her MS thesis work. She presented her thesis work in the annual meeting of BNORC, "Differences in the expression of adiporedoxin and adipokine secretion in human omental and abdominal subcutaneous adipose tissues".
- Train and co-mentor, Simonyte-Sjodin, a post-doctoral fellow from Harvard (currently, assistant professor in Umea University, Sweden), "The effects of RBP4 on adipocyte insulin sensitivity", 2015.
- Co-mentor, Swati Bhattacharya, a MS student in Boston University, 2014 – 2016. Currently, she is working as a clinical coordinator at Boston Medical Center.
- Co-mentor, Christine McInnis, a postdoctoral fellow with Dr. Susan K. Fried (BUMC), 2015-2016. She is currently working as a post-doctoral fellow at Harvard Medical School.
- Co-mentor, Taylor Pickering, a PhD student (BUMC) with Dr. Susan K. Fried, 2013-2017. His thesis project has been published as two papers including the recent publication in Diabetes. He is currently working as a post-doctoral fellow at Boston University School of Medicine funded by a T32 NIH training grant.
- Train and mentor, Varuna Shibad, a research associate (BUMC), 2015-2016. She is currently working as a research associate at Boston University School of Medicine.
- Train users (M. Jager, E. Killion, T. Bowman, C. Cederquist, S. Ding among others) of the Adipocyte Biology and Nutrient Metabolism Core of the NIH funded Boston Nutrition and Obesity Research Center, 2015-2016.
- Trained and mentor a post-doctoral fellow, Arwa Jawadi, and two visiting scholars from Korea, Eunmi Park (Hannam University) and Jinkyung Cho (Sungkyunkwan Univeristy) at Mt. Sinai School of Medicine, Feb. 2019-Sept. 2019.
- Trained an undergraduate student, Nia Miyashro, in in the Dept of HNFAS/ CTAHR University of Hawaii at Manoa, Jan. 2020 – June. 2020
- Currently training an undergraduate student and a PhD Student (Radha Raman Raj), a MS student (Sydney Lofquist) and a high school student, Aarya Mishra, in the Dept of HNFAS/ CTAHR University of Hawaii at Manoa

RESEARCH

RESEARCH INTEREST AND GOAL

Obesity is a very complex disease with multiple etiologies, leading to energy imbalance and increased risks of cardiometabolic diseases. The higher mass of dysfunctional adipose tissue in obesity may cause or exacerbate metabolic diseases (1). Adipose tissues are present in multiple locations. Beyond total fat mass, visceral obesity is independently associated with metabolic disease risk; with visceral fat as more susceptible to metabolic dysfunctions in obesity. In addition to white, more oxidative brown and brite/beige adipocytes are present in adult humans and their amount is

reported to be reduced in obesity (2) and therefore, it is conceivable that increasing the number of brite adipocytes could contribute to energy dissipation and hence, weight control and protection against metabolic complications. My long-term goal is to identify new therapeutic targets to improve adipose tissue functions in obesity. Current research projects are focused on understanding 1) molecular mechanisms that lead to adipose dysfunction in obesity and 2) that mediate the conversion from white adipocyte into brown-like ones.

1) Importance of phospholipid remodeling during conversion from white to brite adipocytes: Brite/beige adipocytes are formed through the recruitment and differentiation of progenitors or the direct conversion from mature white adipocytes. Multiple factors including activation of PPARγ drive a more oxidative program in white human adipocytes, yet molecular details and mechanisms during the conversion are not fully elucidated. Recently, we showed significant structural remodeling, clusters of small lipid droplets surrounded by rearranged mitochondria appear on the surface of the main, central droplet, occurs during rosiglitazone mediated browning of white human adipocytes (*JLR 2019*). Formation of new lipid droplet and mitochondrial rearrangement may require synthesis of new membranes and hence, remodeling of phospholipids. Consistent with this idea, we showed that traicsin C (inhibitor of FA acyl co-A synthesis) blocked the structural remodeling. Furthermore, inhibition of FA activation blocked induction of brite makers, indicating the importance of lipid remodeling in britening program. In our unpublished lipidomics analysis showed that significant remodeling of lipids, induction of several phospholipids and polyunsaturated fatty acids (PUFAs), occurred. I am assessing the importance of remodeling of PUFA-phospholipids in enhancing metabolic flexibility of adipocytes and prevention against obesity and its associated metabolic diseases.

1) Importance of elevated TGFβ signaling in adipose tissue dysfunction in visceral obesity: Expression levels of TGFβ ligands are elevated in obesity. However, the role of TGFβ signaling in adipose tissue functions in human obesity remains poorly understood. In a recent paper, our group showed that high TGFβ ligands produced by adipose progenitors act as cell-autonomous anti-adipogenic factor, contributing to dysfunctions in omental visceral adipose tissue in humans (*Diabetes 2019*). In preliminary experiments, I found that high TGFβ signaling promoted fibrosis and exacerbated adipokine profile in human adipose tissues. Surprisingly, blocking TGFβ signaling with a chemical compound or knockdown of the downstream effector, SMAD2, enhanced adipogenesis and differentiated adipocytes have higher expression levels of UCP1 and PGC1α, indicating that preferential differentiation into brite adipocytes. I am studying the importance of the TGFβ-SMAD2 signaling in fibrosis and adipose endocrine and metabolic functions using in vivo and in vitro approaches.

3) Other Research Interest: I am collaborating with Dr. Fried (Mt. Sinai School of Medicine), my former mentor and long-term collaborator, for the studies of investing the mechanisms that govern sex-dependent depot differences in adipose tissue remodeling capacity and its contribution to metabolic health. In collaborations with Drs. Puri (Ohio University) and Fried, I am investing the importance of lipid droplet proteins (PLIN5 and CIDEA) in the remodeling of lipid droplets and mitochondria and metabolic capacity in adipocytes. I am also collaborating with Drs, N. Moustaind-Moussa (Texas Tech University) and R. Lath (Syracuse University) for the studies of the importance of dietary lipids on adipose tissue health and metabolic diseases and the impact of fraternal nutrition on offspring health. In collaboration with Dr. V Kidambi (Wisconsin Medical College), we are investigating the Role of Adiposity Distribution and MicroRNAs in Obesity Pathogenesis. In addition, I am collaborating with Drs. Nimitphong (Mahidol Univ., Thailand) and Park (Hannam Univ., Korea) for the studies of role of vitamin D in adipose tissue biology.

CONTRIBUTION TO SCIENCE AND AREA OF EXCELLENCE

Nutritional and hormonal regulation of leptin production: Leptin is an adipocyte derived hormone that regulates food intake, energy utilization and immunity. In series of in vitro and in vivo experiments using human adipose tissue explants cultures, adipocytes in culture and rats as model systems, we demonstrate that leptin production is regulated at multiple levels: transcription, translation of mRNAs and secretion (*AJP-EM 2005, JLR 2006, JBC 2007, AJP-EM 2007*) and we were invited to write a review paper, "Integration of Hormonal and Nutrient Signals that Regulate Leptin Synthesis and Secretion", published in *AJP-EM (2009)*. Our study showed that a glucocorticoid is required for high expression of leptin mRNA, insulin increases the efficiency of leptin mRNA translation as well as secretion from the cellular storage, 5'-untranslated region (UTR) of leptin mRNA increases while 3'-UTR depresses leptin translation, and both 5' and 3'-UTR are required for insulin stimulation of leptin mRNA translational efficiency. Activation of adrenergic signaling suppresses leptin production at multiple steps, mediating fasting-suppression of leptin production from adipocytes. Our new work shows that the RNA binding protein TIAR mediates the suppression of leptin signaling the fasted state. Collectively, our work on leptin demonstrates the complexity of signals that allow the adipocyte to respond to nutritional and hormonal cues to regulate system metabolism. The mechanisms we uncovered will undoubtedly apply to the many adipokines produced by adipocytes.

Depot differences in adipose tissue production of adipokines, discovery of novel adipokines and their contribution to metabolic diseases: Adipose tissue produces adipokines and cytokines that regulate systemic energy metabolism. The production of inflammatory cytokines (TNFα, IL-6, IL-1β, CCL2, leptin) is upregulated while expression of adiponectin and omentin, insulin-sensitizing and anti-inflammatory adipokines, is reduced in obesity. In collaborations with Drs. Gong, Yang and Shulidner at University Maryland School of Medicine, we sequenced ~10,000 expressed sequence tags (ESTs) from a human omental fat cDNA library and discovered a novel visceral specific adipokine, omentin (*AJP-EM, 2006*). Further, we showed that ometin may act as insulin sensitizer and that its expression in adipose tissue and serum levels are decreased in human obesity (*Diabetes, 2007*). We compared transcriptome of fat cells to stromal cells of human subcutaneous and omental adipose tissue and discovered that an acute-phase protein, serum amyloid A (SAA), is highly expressed in human adipose tissue (adipocytes) in contrast to its high expression in the liver in rodents. Our study showed that SAA is more abundantly expressed in the subcutaneous than visceral depots and expression levels of SAA in adipose tissues and serum levels are increased in human obesity and may increase C reactive protein production, increasing risks for cardiovascular diseases (*PLoS-Med 2006, Obesity 2014*).

In collaboration with Dr. Kern's research group at the University of Arkansas, we showed that other adipokines including visfatin, retinol binding protein 4 and thrombospondin 1 are also depot dependently expressed and its expression in adipose tissues and serum levels are altered, contributing to the higher risks of insulin resistance and metabolic diseases in human obesity (*JCEM 2006, JCEM 2007, Diabetes 2008*).

The effects of glucocorticoids in depot-specific adipose biology: Glucocorticoids play pleiotropic roles in adipose tissue biology including metabolic and endocrine functions and adipose tissue development. Excess glucocorticoids as seen in Cushing's syndrome, are through to promote fat accumulation preferentially in visceral compared to subcutaneous depots, but the molecular mechanisms involved remain poorly understood. We elucidated the mechanisms through which glucocorticoids regulate adipose tissue function (adipokine production and lipid metabolism) and adipogenesis in different adipose depots. Using the adipose explants organ culture system which

contains multiple cell types, we showed a feedforward regulation of 11-beta hydroxysteroid dehydrogenase in omental but not in subcutaneous adipose tissue that contribute to the preferential fat accumulation in the visceral depot (*Obesity, 2008*). Our studies in newly-differentiated adipocyte in culture that majority of glucocorticoid effects (induction of adipogenesis and adipokine production) are mediated through the type II glucocorticoid receptor rather than type 1 mineralocorticoid receptor (*IJO 2014*).

Gene expression profiling of human omental and subcutaneous adipose tissues treated with dexamethasone, the type II glucocorticoid receptor agonist, identified genes and pathways that are commonly or depot-specifically regulated by glucocorticoids between the depots (*AJP-EM 2011*). Gene set enrichment analysis of transcriptome of omental and subcutaneous human adipose tissues treated with different concentration of dexamethasone identified biological pathways that are affected by glucocorticoids, commonly and depot-specifically between the two depots. Cluster analysis of transcripts that exhibited an interaction of depot and dexamethasone revealed sets of genes for which the responses to dexamethasone differed in magnitude, sensitivity or direction between the two depots as well as mRNAs that responded only in one depot (*PLoS-One 2016*). I am collaborating with Dr. Fried at MSSM to investigate the importance of these findings for the glucocorticoid-mediated regulation of adipose biology, commonly or depot-specifically. We were invited to write a review, "Deconstructing the roles of glucocorticoids in adipose tissue biology and the development of central obesity", published in *BBA (2014)*.

We also demonstrated that glucocorticoid induced leucine zipper (GILZ), a primary target of glucocorticoids identified in our transcriptomics in human adipose tissues, are commonly induced in both depots and at least partially, mediates the effects of glucocorticoids on adipokine production and inflammation in human adipocytes. Expression levels of GILZ are reduced in adipose tissue of human obesity, potentially contributing to the higher inflammation (*JLR 2016*). Our unpublished research in human adipose stem cells showed that GILZ also mediates the proadipogenic effects of glucocorticoids by reducing the anti-adipogenic cytokine signaling pathways (*manuscript in preparation*).

Development of protocols to isolate adipose progenitors, improve their adipogenic degree and their use for gene expression modulation and metabolic studies: Although mouse adipocyte cells lines provide invaluable model systems for mechanistic studies, adipose tissue derived stems cells (ASCs) are also useful for assessing donor- and origin-dependent effects (depot, sex, age, obesity, etc) on cell proliferation and differentiation capacity, which is not possible with cell lines. I developed and optimized the growth and differentiation protocols for human ASCs. In addition, I developed detailed protocols to use newly-differentiated human adipocytes for metabolic studies (lipolysis and glucose transport) and siRNA mediated gene silencing and overexpression of genes of interests. Use of human adipocytes are increasing due to its clinical relevance compared to the mouse cell lines and I have provided our protocols to many investigators both nationally and internationally. Primary cultures of ASCs are heterogeneous in cell populations and therefore, I have developed methods to identify adipocyte progenitor populations with Fluorescence-Activated Cell Sorting and immunoprecipitation with magnetic nanoparticles. I developed and standardized these protocols while working as an assistant core director for the Adipocyte Biology and Nutrient Metabolism Core, Boston Nutrition and Obesity Research Center. These are published as 4 method papers (*Methods in molecular biology 2013, Obesity 2012, ME 2014, Obesity 2014*) and many investigators have been asking the papers. Further, I was invited to write a paper, "Hormonal Regulation of Adipogenesis", in in the prestigious journal, *Compr. Physiol. (2017)*. As an assistant core director, I also provided hands-on training on adipose tissue biology as well as consultation and advice on the experimental design

and data interpretation, greatly broadening the technical capacities of the Core. I also actively participated in the application process for the renewal of BNORC.

Depot differences in adipogenesis and their clinical relevance: During normal growth and in response to overnutrition, adipose tissue expands by increasing the volume of preexisting adipocytes (hypertrophy) or by generating new adipocytes through recruitment and differentiation of adipose progenitors (hyperplasia). The inability to recruit new progenitors and differentiate them into adipocytes results in increases in the size of existing adipocytes and may also results in ectopic fat deposition in other organs including liver and skeletal muscle, which is known to be critical for the development of obesity-related metabolic diseases including insulin resistance. The impaired capacity of visceral compared to subcutaneous adipose tissues to remodel and expand through hyperplasia is thought to account for dysfunctions in the depot and hence, the association of visceral adiposity with insulin resistance and metabolic health. In collaboration with Drs. Wu and Fried, we showed that adipose progenitors from visceral vs. subcutaneous or male vs. female mice exhibit lower adipogenesis and they accumulate in the depot in response to high fat diet induced obesity, contributing to the dysfunctions in the depot as well as systemic metabolism (*AJP-EM 2017*). We found that balance of MMP3, a matrix metalloproteinase that is expressed at much higher levels in inguinal than visceral and female than male mice, and its inhibitor, TIMP4, contribute to the sex-dependent depot differences in adipogenesis. Using fat transplant studies, we are investigating whether intraabdominal or inguinal subcutaneous fat of male vs. female contain intrinsic properties to regulate adipose growth and hence, systemic glucose-insulin metabolism.

Using adipose tissue stem cells derived from human adipose tissues and adipose tissue samples, we also investigated factors governing depot differences in adipose tissue remodeling capacity and function in humans. In a recent paper, we showed that TGFβ signaling is important for the lower hyperplastic remodeling capacity contributing to tissue fibrosis in the omental visceral adipose tissues in human obesity (*Diabetes 2019*). I recently published a review, "TGFbeta Superfamily Regulation of Adipose Tissue Biology in Obesity" in *BBA-DIS (2018).* In collaborations with Dr. Smith using transcriptome and miRNome, our group also showed that developmental heterogeneities between the upper and lower body subcutaneous adipose tissues (*JCEM 2014, Obesity 2017*).

I have been invited to write reviews and one book chapter. I wrote 4 reviews in the topic of adipose depot differences and metabolic health, "Adipose tissue remodeling in pathophysiology of obesity" (*Curr Opin Clin Nutr Metab Care 2010*), "Adipose tissue heterogeneity: Implication of depot differences in adipose tissue for obesity complications" (*Mol Aspects Med 2013*), "Shaping fat distribution: New insights into the molecular determinants of depot- and sex-dependent adipose biology" (*Obesity 2015*), "Sex-dependent Depot Differences in Adipose Tissue Development and Function; Role of Sex Steroids" (*Int Obes Metab Syndr 2017*). Additionally, I wrote "Adipose Tissue in Health and Disease, Chapter 15. Depot-Specific Biology of Adipose Tissues: Links to Fat Distribution and Metabolic Risk" (*Wiley-VCH Verlag GmbH & Co 2010*). These reviews have been highly cited, an additional testament of my contribution to the field.

INVITED LECTURES AND PRESENTATIONS

Aug. 2004 "Feeding and insulin increase leptin production in rat adipose tissue", FASEB summer conference, Colorado, USA. *Oral presentation*

Oct. 2006 "Post-transcriptional modulation of glucocorticoid receptors in human adipose tissue" International Congress of Obesity, Sidney, Australia. *Oral presentation*

May 2008 "Depot-specific effects of glucocorticoid on gene expression in human abdominal subcutaneous and omental adipose tissues", NIH workshop on adipose tissue maintenance and remodeling. Bethesda, MD, USA. *Oral presentation*

May 25, 2010 "Glucocorticoid regulation of adipose tissue biology", Boston Nutrition and Obesity Research Center Adipocyte & Metabolic Study group seminar series. Boston, MA, USA *Oral presentation*

Oct. 2010 "Glucocorticoids Antagonize Tumor Necrosis Factor-alpha Induced Lipolysis in Human Adipocytes", The Obesity Society Annual Meeting, San Diego, USA. *Oral presentation*

April 2013 "1,25(OH)2D3 decreases leptin, IL-6 and SAA expression in human adipocytes: role of vitamin D receptor", Experimental Biology, American Society for Nutrition, Annual Meeting, Boston, USA. *Oral presentation*

Nov. 2014 "Thiazolidinediones induction of brite phenotype in subcutaneous human adipose tissue", The Obesity Society Annual Meeting, Boston, USA. *Oral presentation*

Mar. 13, 2015 "Can we briten human adipocytes?", Center of Animal Biotechnology and Gene Therapy and Department of Biochemistry and Molecular Biology, School of Veterinary Medicine, Universitat Autònoma de Barcelona, Spain

April 08, 2015 "Rosiglitazone Induction of Britening in Human Adipose Tissue", James C. Melby, M.D. Memorial Endocrinology Grand Rounds, Boston University School of Medicine, Boston, MA, USA

Sept. 2015 "Secretory factors produced by cultures of human omental adipose stem cells inhibit adipose differentiation", New York Regional Obesity Forum, New York, NY, USA. *Oral presentation*

Aug. 6, 2016 "Glucocorticoid Regulation of Adipose Inflammation in Obesity", FASEB Science Research Conference on Immunological Aspects of Obesity, Big Sky, Montana, USA.

Nov. 2016 "High Fat Diet-Induced Obesity Downregulates MMP3 to Modulate Depot- and Sex-dependent Adipose Expansion in C57BL/6J Mice", NIH workshop on The Adipose Tissue Niche: Role in Health and Diseases, *Oral presentation, Selected for Travel Award*, NIH, Bethesda, MD, USA

Mar. 28, 2017 "Glucocorticoid-TGFβ cross-talk contributes to the lower adipogenic capacity of human adipose stem cells", Mount Sinai Obesity Forum, Manhattan, NY, USA

April 13, 2017 Diabetes, Obesity and Metabolism Institute Work in Progress Seminar Series, "Resistance to Glucocorticoid Suppression of TGFβ Signaling Pathway Contributes to the Low Adipogenic Capacity of Visceral Adipose Progenitors". Manhattan, NY, USA.

Feb. 26, 2018 Diabetes, Obesity and Metabolism Institute Work in Progress Seminar Series, "Britening of human white adipose tissue", Manhattan, NY, USA.

June 2018 "Reprograming of Human Adipocytes to a Briter Phenotype – Enhanced Fatty Acid Oxidation and Lipid Droplet Remodeling", *Oral Presentation*, American Diabetes Association, 78th Scientific Session, Orlando, FL, USA.

Oct. 16, 2018 "Contribution of sex and depot dependent differences in adipose tissue remodeling capacity to metabolic diseases", Gyeongpuk National University School of Medicine, Center for Developing Treatment for Diabetes and Metabolic Diseases, Daegu, Korea.

Oct. 18, 2018 "Impaired remodeling capacity of visceral adipose tissue in obesity", The Korean Nutrition Society – 2018 Annual Conference, Pyeongchang, Korea.

Oct. 23, 2018 "Lower remodeling capacity in visceral adipose tissues of human obesity", Renowned International Scholar Lecture Series, Pusan National University, Pusan, Korea.

Oct. 24, 2018 "Accumulation of Dysfunctional Adipose Tissues Contributes to Metabolic Diseases in Obesity", Hannam University, Department of Food and Nutritional Sciences, Daejeon, Korea.

March 04, 2019 Diabetes, Obesity and Metabolism Institute Work in Progress Seminar Series, "Structural and metabolic remodeling during conversion from white into briter human adipocytes", Manhattan, NY, USA.

June 25, 2019 "Harnessing Adipose Tissue Functions to Improve Systemic Metabolism", Pusan National University, Pusan, Korea.

Oct. 29, 2019 "Structural and Metabolic Remodeling during Britening of White Adipocytes", Texas Tech University, TX, USA.

Dec. 17, 2021 "Effects of n-3 fatty acids on adipocyte functions", Chungnam Nat'l University, Daejoeon, Korea

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TEXTBOOK CHAPTER:

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