BIOGRAPHICAL SKETCH

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NAME: **Erin E. Kershaw, MD**

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

POSITION TITLE: Associate Professor of Medicine, University of Pittsburgh, Pittsburgh, PA USA

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	Completion Date	FIELD OF STUDY
Cornell University, Ithaca, NY	B.A.	05/1991	Biology, Nutrition
Cornell University Medical College, New York, NY	M.D.	05/1997	Medicine (Research Honors)
New York Presbyterian Hospital-Cornell Medical Center, New York, NY	Intern & Resident	06/2003	Internal Medicine
Beth Israel Deaconess Medical Center, Boston, MA	Fellow	06/2003	Endocrinology

A. Personal Statement

I have broad experience in the field of endocrinology, diabetes, and metabolism including over 25 years specifically devoted to clinical and scientific efforts to understand obesity, diabetes, and their complications. I have developed specific expertise in key research areas including metabolic assessment of cells, mice, and humans. My research program focuses on defining mechanisms by which lipid and steroid metabolism contribute to normal metabolism and disease. Most recently, my research efforts have focused on pathways of triacylglycerol hydrolysis (lipolysis). Another major focus of my research program is to identify and characterize proteins and pathways that contribute to metabolic disease. These efforts fall into two main areas: 1) characterizing novel adipocyte-secreted factors and their relationship to metabolic disease in humans, and 2) characterizing novel genes/loci linked to metabolic disease in humans. We use a combination of molecular, cellular, physiological, and translational approaches. Our ultimate goal is to develop more effective strategies for prevention and treatment of obesity, diabetes, and their complications. I have successfully competed for and administered grants to fund my research including grants from the Howard Hughes Medical Institute, American Diabetes Association, and the National Institutes of Health. I also have experience serving in large, multi-institutional research consortiums (i.e. U01 AR071130-01, UG3 DK119973). I currently hold several leadership roles, including Chief of the Division of Endocrinology, Associate Program Director for the Clinical Endocrinology Fellowship Program, and Oversight/Steering Committee Member for the T32 Training Program in Endocrinology, and Metabolism. This experience is enriched by clinical expertise and board certification in 1) Endocrinology, Diabetes, and Metabolism, 2) Clinical Lipidology, and 3) Obesity Medicine. Thus, I have demonstrated a record of successful and productive research, clinical activity, and leadership in the field of endocrinology, diabetes, and metabolism.

B. Positions and Honors

Positions and Employment

1993-1995 **HHMI Medical Student Research Fellow**, Leibel Lab, The Rockefeller University, NY, NY
1996-1997 **Medical Student Research Fellow**, Gershengorn Lab, Cornell Medical College, NY, NY
1997-2000 **Intern and Resident in Internal Medicine**, Department of Medicine, New York Presbyterian Hospital – Cornell Medical Center, NY, NY
1999-2000 **Resident Research Fellow**, Stoffel Lab, The Rockefeller University, NY, NY
2000-2003 **Clinical and Research Fellow in Endocrinology and Metabolism,** Division of Endocrinology, Department of Medicine, Beth Israel Deaconess Medical Center, Joslin Diabetes Center, and Harvard Medical School, Flier Lab, Boston, MA

2003-2008 **Instructor in Medicine**, Division of Endocrinology, Beth Israel Deaconess Medical Center, Joslin Diabetes Center, and Harvard Medical School, Boston, MA
2008-2014 **Assistant Professor of Medicine**, Division of Endocrinology, University of Pittsburgh, Pittsburgh, PA
2013- **Faculty Member**, Interdisciplinary Biomedical Graduate Program, Molecular Genetics and Developmental Biology, University of Pittsburgh, Pittsburgh, PA
2014- **Associate Professor of Medicine (with tenure 2017)**, Division of Endocrinology, University of Pittsburgh, Pittsburgh, PA
2016- **Chief**, Division of Endocrinology, University of Pittsburgh, Pittsburgh, PA
2017- **Endowed Chair** of Obesity and Diabetes Research, Department of Medicine, Division of Endocrinology, University of Pittsburgh, Pittsburgh, PA

Relevant Research Related Positions and Memberships

Pittsburgh Diabetes Institute (PDI), University of Pittsburgh, Pittsburgh, PA; Vascular Medicine Institute (VMI), University of Pittsburgh, Pittsburgh, PA; Center for Metabolism/Mitochondrial Medicine (C3M), University of Pittsburgh, Pittsburgh, PA; Pittsburgh Liver Research Center (PLRC), University of Pittsburgh, Pittsburgh, PA; Healthy Lifestyles Institute (HLI), University of Pittsburgh, Pittsburgh, PA

Service on Grant Review Panels

07/2010	*Ad hoc* reviewer	NIH/NIDDK, 2010/07 ZDK1 GRB-7 (O3)
10/2011	*Ad hoc* reviewer	NIH/NIDDK, Cellular Aspects of Diabetes and Obesity (CADO)
03/2012	*Ad hoc* reviewer	NIH/NCI, 2012/05 ZCA1 SRLB-D (M1) R
03/2013	*Ad hoc* reviewer	NIH/NIGMS, 2013/05 ZGMI TWD-C (CC)
06/2013	*Ad hoc* reviewer	NIH/NHLBI, 2013/10 ZHL1 PPG-R (01)1
02/2014	*Ad hoc* reviewer	NIH/NCCAM, 2014/05 ZAT1 PK (29) P
03/2014	*Ad hoc* reviewer	NIH/NIDDK, 2014/03 DDK-B
05/2014	*Ad hoc* reviewer	NIH/NCCAM**,** 2014/05 ZAT1 PK (29) P
03/2016	*Ad hoc* reviewer	NIH/NHLBI ZHL1 CSR-R (M2) 1
03/2016	*Ad hoc* reviewer	Howard Hughes Medical Institute International Scholars Program
16/2016	*Ad hoc* reviewer	NIH/NIDDK, Integrative Nutrition and Metabolic Processes (INMP)
10/2016	*Ad hoc* reviewer	NIH/NIDDK, Integrated Physiology of Obesity and Diabetes (IPOD)
07/2017	*Ad hoc* reviewer	NIH/NIDDK, 2017/10 ZRG1 CADO B (90) S
07/2017-	Standing reviewer	NIH/NIDDK, DDK-B: Diabetes, Endocrinology, and Metabolic Diseases B

Professional Certifications

2005- American Board of Internal Medicine – Endocrinology, Diabetes, & Metabolism Certification
2015- American Board of Clinical Lipidology – Clinical Lipidology Certification
2015- American Board of Obesity Medicine – Obesity Medicine Certification

Professional Memberships

American Diabetes Association (ADA)**.** The Obesity Society (TOS)**,** Endocrine Society (ES)**,** National Lipid Association (NLA)**,** Member, American Heart Association (AHA)

Honors

1991 Cornell University, Departmental Honors for graduating in top 10% of the class
1991 Cornell Alumni Program Research Award
1991 Golden Key National Honor Society
1992 Cornell University Medical College, David P. Barr Research Fellowship
1993-1994 Howard Hughes Medical Institute (HHMI), Medical Student Research Award (2 years)
1994 Cornell University Medical College, Dr. Harold Lamport Biomedical Research Award
1995 Cornell University Medical College, Dean's Research Award
1995-1996 Howard Hughes Medical Institute (HHMI), Award for Continuation of Medical Studies (2 years)
1996 Cornell University Medical College, Alpha Omega Alpha Medical Honor Society
1997 Cornell University Medical College, Medical Doctorate with Honors in Research
1997 Cornell University Medical College, Janet M. Glasgow Memorial Achievement Award
1997 The Endocrine Society, Honorary Membership Award for Endocrine Research and Education
1999 New York Presbyterian Hospital, David E. Rogers Memorial Research Award
2002 Endocrine Fellows Foundation, Endocrine Fellow Research Award

2009-2014 Howard Hughes Medical Institute (HHMI), Physician-Scientist Early Career Award (5 years)
2010 University of Pittsburgh, Department of Medicine Junior Scholar Award
2011 University of Pittsburgh, Winters Foundation Award
2012 University of Pittsburgh, Senior Vice Chancellor's Research Seminar Invited Speaker

C. Contributions to Science

1. As a K08-funded Junior Faculty (2003-2008), my research focused on adipocyte-specific glucocorticoid metabolism by 11β-hydroxysteroid dehydrogenases (11βHSDs). Although systemic glucocorticoid excess has profound metabolic effects, no clear abnormalities in serum glucocorticoids are evident in obesity or metabolic syndrome. We hypothesized that tissue-specific *intracellular* glucocorticoid metabolism by 11βHSDs contributes to metabolic phenotypes. We demonstrated that *adipocyte*-specific glucocorticoid activation by 11βHSDs increases susceptibility to metabolic syndrome, whereas *adipocyte*-specific glucocorticoid inactivation by 11βHSDs decreases susceptibility to metabolic syndrome (a). These studies established the importance of *intracellular* glucocorticoid metabolism in obesity and metabolic disease. Furthermore, as a result of this work, we identified novel glucocorticoid-regulated genes in adipose tissue that contribute to metabolic syndrome. These proteins included novel proteins in the patatin-like phospholipase (PNPLA) family (i.e. adipose triglyceride lipase and adiponutrin) that formed the foundation of my subsequent work (b, c).
   a. **Kershaw EE**, Morton NM, Dhillon H, Ramage L, Seckl JR, Flier JS. Adipocyte-specific glucocorticoid inactivation protects against diet-induced obesity. Diabetes. **2005** Apr; 54(4):1023-31. PMID: 15793240, [PMCID: PMC2819172].
   b. **Kershaw EE**, Hamm JK, Verhagen LAW, Peroni O, Katic M, Flier JS. Adipose triglyceride lipase: function, regulation by insulin, and comparison with adiponutrin. Diabetes. **2006** Jan; 55(1):148-57. PMID: 16380488. [PMCID: PMC2819178].
   c. **Kershaw EE**, Schupp M, Guan HP, Gardner NP, Lazar MA, Flier JS. PPARγ regulates adipose triglyceride lipase in adipocytes in vitro and in vivo. Am J Physiol Endocrinol Metab. **2007** Dec; 93(6):E1736-45. Epub 2007 Sep 11. PMID: 17848638. [PMCID: PMC2819189].

2. As an independently-funded (R03, R01, and HHMI Early Career Award) Principal Investigator, my research has focused on the role of intracellular lipid metabolism in glucose homeostasis and insulin action, with a special emphasis on novel lipid metabolizing proteins of the patatin-like phospholipase domain containing protein (PNPLA) family. One member of this family, Adipose Triglyceride Lipase (ATGL/PNPLA2), is the rate-limiting enzyme in triacyglycerol hydrolysis, arguably one of the most fundamental processes in metabolism. My work contributed to the early understanding of the regulation, function, and physiological reliance of this important protein, particularly in adipose tissue (a, d) and skeletal muscle (a, b, c) metabolic homeostasis.
   a. Kienesberger PC, Lee D, Pulinilkunnil T, Brenner DS, Cai L, Magnes C, Koefeler HC, Streith IE, Rechberger GN, Haemmerle G, Flier JS, Zechner R, Kim YB, and **Kershaw EE**. Adipose triglyceride lipase deficiency causes tissue-specific changes in insulin signaling. J Biol Chem. **2009** Oct 30; 284(44):30218-29. doi: 10.1074/jbc.M109.047787. Epub 2009 Aug 31. PMID: 19723629. [PMCID: PMC2781577].
   b. Sitnick MT*, Basantani MK*, Cai L*, Schoiswohl G, Yazbeck CF, Distefano G, Ritov V, Delany JP, Schreiber R, Stolz DB, Gardner NP, Kienesberger PC, Pulinilkunnil T, Zechner R, Goodpaster BH, Coen P, and **Kershaw EE.** Skeletal muscle triacylglycerol hydrolysis does not influence metabolic complications of obesity. Diabetes. **2013** Oct; 62(10):3350-61. doi: 10.2337/db13-0500. Epub 2013 Jul 8. PMID: 23825334. [PMCID: PMC3781480]. *Authors contributed equally to this work. ***Note: Cover***.
   c. Dube JJ, Sitnick MT, Schoiswohl G, Wills R, Basantani BK, Cai L, and **Kershaw EE**. Adipose triglyceride lipase (ATGL) deletion from adipocytes, but not skeletal myocytes, impairs acute exercise performance in mice. Am J Physiol Endocrinol Metab. **2015** May 15; 308(10):E879-90. doi: 10.1152/ajpendo.00530.2014. Epub 2015 Mar 17. PMID: 25783895. [PMCID: PMC4436997].
   d. Schoiswohl G, Stefanovic-Racic M, Menke MN, Yazbeck CF, Cai L, Basantani MK, Sitnick MT, Wills R, Stolz DB, O'Doherty RM, **Kershaw EE**. Impact of reduced adipocyte lipolysis on obesity-associated inflammation and insulin resistance in male mice. Endocrinology. **2015** Oct; 156(10):3610-24. doi: 10.1210/en.2015-1322. Epub 2015 Jul 21. PMID: 26196542. [PMCID: PMC4588821].

3. In conjunction with the above work related to ATGL/PNPLA2 in adipose tissue and skeletal muscle, I have collaborated with several prominent investigators in the field to understand the tissue-specific effects of ATGL action (and lipolysis in general) on cardiac muscle (8 publications to date) as well as other tissues / cell types including immune cells (J Leukocyte Biol 2015; Am J Physiolo Endocrinol Metab 2018), intestines (J Lipid Res 2013), liver (J Hepatology 2015; JCI Insight 2017; Cell Metab 2017; Am J Physiolo Endocrinol Metab 2018), kidneys (J Lipid Res 2017), and bone (JCI Insight 2017). With respects to cardiac muscle, our collaborative work constitutes the majority of literature on the impact of ATGL action on the heart. One of the most

impactful findings of this work is that ATGL-mediated fat catabolism regulates cardiac mitochondrial function via PPARα and PGC-1α (a), suggesting that ATGL action generates a lipid ligands for PPAR nuclear transcription factors. We have also shown that ATGL also has PPARα-independent effects on cardiac muscle function (d). We have collaboratively demonstrated that increasing ATGL action in cardiac muscle improves many types of cardiomyopathies including pressure overload (b) and diabetic (c) cardiomyopathy. Together these data support an important role for ATGL in cardiac muscle metabolism and function. This work also underscores my ability to collaborate with diverse groups internationally to promote scientific knowledge in my field (25 ATGL-related publications to date).

a. Haemmerle G, Moustafa T, Woelkart G, Kotzbeck P, Büttner S, Schmidt A, van de Weijer T, Hesselink M, Kienesberger P, Zierler K, Schreiber R, Eichmann T, Kolb D, Schweiger M, Kumari M, Eder S, Schoiswohl G, Wonsiriroj N, Jäger D, Pollak N, Preiss-Landl K, Kolbe T, Rülicke T, Pieske B, Trauner M, Lass A, Zimmermann R, Hoefler G, Cinti S, **Kershaw EE**, Schrauwen P, Madeo F, Mayer B, and Zechner R. ATGL-mediated fat catabolism regulates cardiac mitochondrial function via PPARα and PGC-1α. Nat Med. 2011 Aug; 17(9):1076-85. doi: 10.1038/nm.2439. PMCID: PMC3244833.
b. Kienesberger PC, Pulinilkunnil T, Sung MY, Haemmerle G, **Kershaw EE**, Young ME, Light PE, Oudit GY, Zechner R, Dyck JRB. Myocardial ATGL overexpression decreases the reliance on fatty acid oxidation and protect against pressure overload-induced cardiac dysfunction. Mol Cell Bio. **2011** Feb; 32(4):740-50. doi: 10.1128/MCB.06470-11. Epub 2011 Dec 12. PMCID: PMC3272983.
c. Pulinilkunnil T, Kienesberger PC, Negendran J, Waller TJ, Young M, **Kershaw EE**, Korbutt G, Haemmerle G, Zechner R, Dyck JRB. Myocardial adipose triglyceride lipase overexpression protects diabetic mice from the development of lipotoxic cardiomyopathy. Diabetes. **2013** May; 62(5):1464-77. doi: 10.2337/db12-0927. Epub 2013 Jan 24.PMCID: PMC3636613.
d. Kienesberger PC, Pulinilkunnil T, Nagendran J, Young ME, Bogner-Strauss JG, Hackl H, Khadour R, Heydari E, Haemmerle G, Zechner R, **Kershaw EE***, Dyck JR*. Early structural and metabolic cardiac remodelling in response to inducible adipose triglyceride lipase ablation. Cardiovasc Res. **2013** Aug; 99(3):442-51. doi: 10.1093/cvr/cvt124. Epub 2013 May 25. PMCID: PMC3718322. *Co-last, Co-corresponding authors.

4. In addition to the above work related to ATGL/PNPLA2, my work has also addressed the regulation, function, and physiological relevance of its closest homolog, Adiponutrin/PNPLA3. My early work reported the nutritional and hormonal regulation of Adiponutrin/PNPLA3 in comparison with ATGL/PNPLA2 (a). I subsequently generated and characterized a murine global Adiponutrin/PNPLA3 knockout mouse (PNPLA3-KO). While this work was underway, Helen Hobbs' group identified genetic variation in PNPLA3 as a major determinant of non-alcoholic fatty liver disease (NAFLD) in humans (Nat Genet 2008). I subsequently showed that PNPLA3-KO mice surprisingly did not develop overt liver-specific or systemic metabolic abnormalities (b), suggesting that either the human genetic variant did not generate disease due to loss of function OR that the function of PNPLA3 in mice was different from humans. My subsequent collaborative work with Rudi Zechner's group demonstrated that Adiponutrin/PNPLA3 functions as a nutritionally regulated lysophosphatidic acid acyltransferase (c). This work contributed to the understanding of one of the strongest known biomarkers for hepatic steatosis, inflammation, and fibrosis in humans.
   a. **Kershaw EE**, Hamm JK, Verhagen LAW, Peroni O, Katic M, Flier JS. Adipose triglyceride lipase: function, regulation by insulin, and comparison with adiponutrin. Diabetes. **2006** Jan; 55(1):148-57. PMID: 16380488. [PMCID: PMC2819178].
   b. Basantani MK, Sitnick MT, Cai L, Brenner DS, Gardner NP, Li JZ, Schoiswohl G, Yang K, Kumari M, Gross RW, Zechner R, and **Kershaw EE**. Pnpla3/Adiponutrin deficiency in mice does not contribute to fatty liver disease or metabolic syndrome. J Lipid Res. **2011** Feb; 52(2):318-29. doi: 10.1194/jlr.M011205. Epub 2010 Nov 9. PMID: 21068004. [PMCID: PMC3023552].
   c. Kumari M, Schoiswohl G, Poeschl M, Cornaciu I, Rangrez AY, Eder S, Oberer M, Haemmerle G, Lass A, **Kershaw EE**, Zimmermann R, and Zechner R. Adiponutrin (PNPLA3) functions as a nutritionally regulated lysophosphatidic acid acyltransferase. Cell Metab. **2012** May 2; 15(5):691-702. doi: 10.1016/j.cmet.2012.04.008. PMID: 22560221. [PMCID: PMC3361708].

5. My research program increasingly includes more translational work in humans by evaluating the relationship between biomarkers and/or genetic risk variants and human metabolic disease. Adipocyte-secreted proteins (adipokines) are well-known to have diverse metabolic effects and also serve as potential therapeutic targets. However, the function and physiological relevance of many adipokines remains poorly understood. To address these issues, we evaluate serum and/or tissue adipokines in human subjects who are very well-characterized for metabolic phenotypes, both before and after relevant interventions (i.e. diet, exercise) intervention. In this way, we are able link scientific findings in rodent models to human metabolic disease. For example, we have recently linked serum Autotaxin, a lysopholipase implicated in rodent insulin resistance, to metablic phenotypes in humans (a,b). We have also evaluated the relationship between serum Wnt pathways

modulators to metabolic phenotypes in humans (c). Most recently, we are working to characterize a novel obesity/diabetes risk variant in CREBRF in humans (d) using cell/rodent models.

a. Rachakonda VP, Reeves VL, Aljammal J, Wills RC, Trybula JS, DeLany JP, Kienesberger PC, and **Kershaw EE**. Serum autotaxin in independently associated with hepatic steatosis in severely obese women. Obesity. **2015** May; 23(5):965-72. doi: 10.1002/oby.20960. Epub 2015 Apr 10. PMID: 25865747. [PMCID: PMC441467].
b. Reeves VL, Trybula JS, Wills RC, Goodpaster BH, Dube JJ, Kienesberger PE, **Kershaw EE**. Serum autotaxin/ENPP2 correlates with insulin resistance in older obese humans. Obesity. **2015** Dec; 23(12):2371-6. doi:10.1002/oby.21232. Epub 2015 Nov 2. PMID: 26727116. [PMCID: PMC4700540].
c. Ali H, Zmuda JM, Cvejkus RK, **Kershaw EE**, Kuipers AL, Oczypok EA, Wheeler V, Bunker CH, Miljkovic I. Wnt Pathway Inhibitor DKK1: A Potential Novel Biomarker for Adiposity. J Endocr Soc. **2019** Jan 3;3(2):488-495. Doi: 10.1210/js.2018-00325. eCollection 2019 Feb 1. PMID: 30746507. [PMCID: PMC6364619].
d. Minster RL, Hawley NL, Su CT, Sun G, **Kershaw EE**, Chen H, Buhule OD, Lin J, Reupena MS, Viali S, Naseri T, Urban Z, Deka R, Weeks DE, McGarvey ST. A thrifty variant in CREBRF strongly influences body mass index in Samoans. Nat Genet. **2016** Sep; 48(9):1049-54. doi: 10.1038/ng.3620. Epub 2016 Jul 25. PMID: 27455349. [PMCID: PMC5069069].

Complete List of Published Work in My Bibliography [**Link**]

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01 DK093093-06 (NIH/NHLBI) **McGarvey (PI)** **Dates: 07/01/16-06/30/20**
Title: Integrated cellular, mouse, and human research on a novel missense variant influencing adiposity
Description: The goals of this project are to characterize a novel human obesity risk variant.
Role: Key personnel / Significant Contributor / **Subcontract PI**

1-17-IBS-128 (ADA) **Kershaw (PI)** **Dates: 01/01/17-12/31/19**
Title: Mechanisms by which a novel human obesity-risk variant protects against diabetes
Description: The goal of this project are to identifying mechanisms by which a novel human obesity-risk variant protects against diabetes using cell and animal models.
Role: Key personnel / Significant Contributor / **PI**

U01 AR071130-01 (NIH Common Fund) **Jakicic (PI)** **Dates: 01/01/17-12/31/22**
Title: Molecular Transducers of Physical Activity Clinical Centers (MoTrPAC)
Description: The goal of this project is to serve as a clinic center that will implement physical activity protocols and collect data/biospecimens for the Molecular Transducers of Physical Activity in Humans Consortium.
Role: Key personnel / Significant Contributor / **Subcontract PI**

R01 DK112962 (NIH/NIDDK) **McGarvey/DeLaney (Co-PIs)** **Dates: 01/01/18-12/31/23**
Title: Impact of the CREBRF R457Q variant on energy expenditure, intake, and substrate utilization in humans
Description: The goal of this project is to determine the impact of a novel obesity risk variant on energy expenditure, energy intake, energy substrate metabolism, and body composition in Samoans.
Role: Key personnel / Significant Contributor / **Subcontract PI**

UG3 DK119973 (NIH/NIDDK) **Taylor (PI)** **Dates: 09/20/18-07/31/20**
Title: Human microphysiological systems disease model T2DM starting with liver and pancreatic islets
Description: The goal of this project is to develop organ-on-chip technology and protocols to model T2DM.
Role: Key personnel / Significant Contributor / Co-I

R01 AG059416 (NIH/NIA) **Cummings/Newman (PI)** **Dates: 09/20/18-07/31/21**
Title: Study of Muscle Mobility and Aging (SOMMA)
Description: The goal of this project is to understand the molecular/biological basis for mobility loss with aging.
Role: Key personnel / Significant Contributor / **Subcontract PI**

Pittsburgh Foundation **Kershaw (PI)** **Dates: 09/01/18-08/31/20**
Title: Overcoming insulin deficiency and resistance to reduce diabetes risk
Description: The goal of the project is to identify novel approaches to target insulin deficiency and resistance to improve diabetes risk.
Role: Key personnel / Significant Contributor / **PI**