

BIOGRAPHICAL SKETCH

NAME: PETERSON, LINDA

POSITION TITLE: Professor of Medicine and Radiology

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	END DATE	FIELD OF STUDY
Georgetown University, Washington D.C.	BS	05/1986	Biology
Washington University School of Medicine, Saint Louis, Missouri	MD	06/1990	Medicine
Barnes Hospital, Saint Louis, Missouri	Resident	06/1993	Internal Medicine
Barnes Hospital, Saint Louis, Missouri	NIH training grant	06/1996	Fellow in Cardiology

A. Personal Statement

The overriding goal of my research program is to investigate how abnormal lipid metabolism in humans is linked with cardiac dysfunction. Early in my career, I performed outcomes research in hundreds of my patients with cardiac dysfunction and heart failure (HF), showing the effects of beta-blocker therapy on the predictive value of VO₂max testing and timing of transplantation. Later, I investigated the effects of excessive myocardial fatty acid uptake, utilization, oxidation, and total oxidation on the human heart. These metabolic perturbations are accompanied by cardiac dysfunction. Furthermore, my research has shown that weight loss in obese subjects decreases myocardial fatty acid metabolism requirements and that this is related to improvements in cardiac function. Because of these links between excessive myocardial fatty acid uptake/utilization with cardiac dysfunction, I have worked with the lipidomics team here at Washington U. since 2005 investigating the plasma lipidome and its relation to cardiovascular disease (CVD). We have worked together in the validation of a high-throughput mass spectrometry method for the quantification of particular lipid species: ceramides and sphingolipids, which have been implicated in lipotoxicity. We have shown that gastric bypass-induced weight loss or a diet rich in medium chain fatty acids alters the plasma lipidome and improves cardiac structure/function. Most recently, as a P20 Metabolomics Center, we have worked collaboratively with investigators from the Framingham Heart Study (FHS) and the Study of Health in Pomerania (SHIP) study to evaluate the value of a ratio of specific ceramide species for the prediction of CVD. We have shown that a ratio of lower plasma ceramide 24:0/16:0 predicts incident CVD, coronary heart disease (CHD), HF, and overall mortality in the FHS and/or SHIP cohorts even after accounting for known risk factors. We also have preliminary data from these community-based cohorts showing these plasma ceramides to be heritable and that there are specific single nucleotide-polymorphisms (SNPs) that associate with ceramide 24:0. I was also head of the Administrative Core for the five P20 Centers. I am well-qualified to be a Primary Investigator on this current project given my experience in human lipidomics, myocardial lipid metabolism, and cardiac dysfunction research. Together, our research team will extend our findings on ceramides to patients with heart failure with preserved ejection fraction (HFpEF) by studying samples and data from the TOPCAT trial. We will further evaluate the genetic underpinnings of these ceramides and their ratio in the TOPCAT patients.

- Peterson LR, Xanthakis V, Stevenson M, Jiang H, Jiang X, Ory DS, Dorr M, Ramachandran SV, Schaffer JE. Plasma very long chain ceramides and risk of cardiovascular events. *J Am Heart Assn* (2018 May 3;7(10). pii: e007931. doi: 10.1161/JAHA.117.007931.
- Nwabuo C, Duncan M, Xanthakis V, **Peterson LR**, Mitchell GF, McManus D, Cheng S, Vasan RS. Association of circulating ceramides with cardiac structure and function in the general population: The Framingham Heart Study. *JAMA* 2019; 8 (19), e013050. PMID: 31549564, PMCID:PMC6806035.
- Walker ME, Xanthakis V, **Peterson LR**, Duncan MS, Lee J, Ma J, Bigornia, Moore LL, Quatromoni PA, Vasan RS, Jacques PF. Dietary patterns, ceramide ratios, and risk of all-cause and cause-specific mortality: the Framingham Offspring Study *J of Nutr* 2020;150:2994-3004.

4. Jiang H, Hsu FF, Farmer MS, Peterson LR, Schaffer JE, Ory DS, Jiang X. Development and validation of LC-MS/MS method for determination of very long acyl chain (C22:0 and C24:0) ceramides in human plasma. *Anal Bioanal Chem.* 2013 Sep;405(23):7357-65. PubMed Central PMCID: PMC3766747.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

- 2023 - President, Society for Heart and Vascular Metabolism
2021 - Study Section Member (CCHS), National Institutes of Health
2020 - Grant Reviewer, Dutch Heart Foundation
2020 - 2020 Study Section Member (CICS), National Institutes of Health
2018 - Editorial Board Member, *Circulation: Cardiovascular imaging*
2017 - Professor of Medicine and Radiology, Washington University School of Medicine, Saint Louis, MO
2016 - 2019 Editorial Board Member, *Diabetes*
2016 - 2019 Board Member, Society for Heart and Vascular Metabolism
2014 - Member, National Governing Committee for AHA Awards and Lectures, American Heart Association
2013 - 2014 President, Academic Women's Network, Saint Louis, MO
2012 - 2016 Young Investigators Award Committee, American Heart Association
2011 - 2011 Grant Reviewer, U01, National Institutes of Health (NIH)
2010 - 2017 Grant Reviewer, *Diabetes U.K. Association*
2008 - Director, Cardiac Rehabilitation, Washington University School of Medicine, Saint Louis, MO
2008 - 2016 Editorial Board Member, *Circulation*
2007 - Fellow, American Heart Association
2007 - 2017 Associate Professor of Medicine and Radiology, Washington University School of Medicine, MO
2007 - 2009 Abstract Grader, American Heart Association
1998 - Fellow, American Society of Echocardiography
1998 - 2007 Assistant Professor of Medicine, Washington University School of Medicine, MO
1996 - 1998 Instructor in Medicine, Washington University School of Medicine, Saint Louis, MO
1995 - Fellow, American College of Cardiology

Honors

- 2020 - 2021 Selected for and attending the "2020-2021 Clinical Trials Research: Upping Your Game Program", American College of Cardiology
2014 - 2014 Mentoring Award, Academic Women's Network, Washington U. School of Medicine
2013 - 2013 Alpha Omega Alpha, Washington U. School of Medicine
2013 - 2013 Distinguished Alumni Scholarship Honoree, Washington U Medical Center Alumni
1997 - 1997 Winner, Amersham award, American Society of Nuclear Medicine
1994 - 1994 Excellence in clinical practice, Syntex
1994 - 1994 Knowlton incentive for excellence award, Washington University School of Medicine
1993 - 1993 Resident teaching award, Washington University School of Medicine
1993 - 1993 Winner, Poster contest, National American College of Physicians' Poster Competition
1986 - 1986 Magna cum laude, Georgetown University
1986 - 1986 Francis Graham Medal of Academic and Athletic Achievement, Georgetown University
1982 - 1982 Valedictorian, Appleton High School-West

C. Contribution to Science

1. My earliest contribution to science was to enroll a large number of heart failure patients (N= 540) in a prospective observational study in order to determine the prognostic value of whole body oxygen consumption testing and new cut-points for timing of transplantation in the beta-blocker era.
 - a. Stolker JM, Heere B, Geltman EM, Schechtman KB, Peterson LR. Prospective comparison of ventilatory equivalent versus peak oxygen consumption in predicting outcomes of patients with heart failure. *Am J Cardiol.* 2006 Jun 1;97(11):1607-10. PubMed PMID: 16728223; NIHMSID: NIHMS205118.
 - b. Peterson LR, Schechtman KB, Ewald GA, Geltman EM, de las Fuentes L, Meyer T, Krekeler P, Moore ML, Rogers JG. Timing of cardiac transplantation in patients with heart failure receiving beta-adrenergic blockers. *J Heart Lung Transplant.* 2003 Oct;22(10):1141-8. PubMed PMID: 14550824; NIHMSID: NIHMS327214.
 - c. Peterson LR, Schechtman KB, Ewald GA, Geltman EM, Meyer T, Krekeler P, Rogers JG. The effect of beta-adrenergic blockers on the prognostic value of peak exercise oxygen uptake in patients with heart failure. *J Heart Lung Transplant.* 2003 Jan;22(1):70-7. PubMed PMID: 12531415.
2. My multimodality translational imaging research helped define the myocardial metabolism abnormalities in human heart failure, obesity, and diabetes. Furthermore, my group's clinical trials evaluated the effects of different interventions on myocardial metabolism.
 - a. Kadkhodayan A, Lin CH, Coggan AR, Kisrieva-Ware Z, Schechtman KB, Novak E, Joseph SM, Dávila-Román VG, Gropler RJ, Dence C, Peterson LR. Sex affects myocardial blood flow and fatty acid substrate metabolism in humans with nonischemic heart failure. *J Nucl Cardiol.* 2017 Aug;24(4):1226-1235. PubMed Central PMCID: PMC5517366.
 - b. Airhart S, Cade WT, Jiang H, Coggan AR, Racette SB, Korenblat K, Spearie CA, Waller S, O'Connor R, Bashir A, Ory DS, Schaffer JE, Novak E, Farmer M, Waggoner AD, Dávila-Román VG, Javidan-Nejad C, Peterson LR. A Diet Rich in Medium-Chain Fatty Acids Improves Systolic Function and Alters the Lipidomic Profile in Patients With Type 2 Diabetes: A Pilot Study. *J Clin Endocrinol Metab.* 2016 Feb;101(2):504-12. PubMed Central PMCID: PMC4880128.
 - c. Lin CH, Kurup S, Herrero P, Schechtman KB, Eagon JC, Klein S, Dávila-Román VG, Stein RI, Dorn GW 2nd, Gropler RJ, Waggoner AD, Peterson LR. Myocardial oxygen consumption change predicts left ventricular relaxation improvement in obese humans after weight loss. *Obesity (Silver Spring).* 2011 Sep;19(9):1804-12. PubMed Central PMCID: PMC3398694.
 - d. Peterson LR, Herrero P, Schechtman KB, Racette S, Waggoner AD, Kisreiva-Ware, Zulia, Dence, C, Klein S, Marsala J, Timothy Meyer, Gropler RJ: Effect of obesity and insulin resistance on myocardial substrate metabolism and efficiency in young women. *Circulation* 2004;109:2191-2196.
3. My group was the first to demonstrate that men and women differ in their myocardial perfusion and metabolic profile. We have shown this in patients with heart failure (see Kadkhodayan et al. above) as well as in normal healthy humans and in patients with obesity or diabetes.
 - a. Peterson LR, Herrero P, Coggan AR, Kisrieva-Ware Z, Saeed I, Dence C, Koudelis D, McGill JB, Lyons MR, Novak E, Dávila-Román VG, Waggoner AD, Gropler RJ. Type 2 diabetes, obesity, and sex difference affect the fate of glucose in the human heart. *Am J Physiol Heart Circ Physiol.* 2015 Jun 15;308(12):H1510-6. PubMed Central PMCID: PMC4469879.
 - b. Peterson LR, Saeed IM, McGill JB, Herrero P, Schechtman KB, Gunawardena R, Recklein CL, Coggan AR, DeMoss AJ, Dence CS, Gropler RJ. Sex and type 2 diabetes: obesity-independent effects on left ventricular substrate metabolism and relaxation in humans. *Obesity (Silver Spring).* 2012 Apr;20(4):802-10. PubMed Central PMCID: PMC3314727.
 - c. Peterson LR, Soto PF, Herrero P, Mohammed BS, Avidan MS, Schechtman KB, Dence C, Gropler RJ. Impact of gender on the myocardial metabolic response to obesity. *JACC Cardiovasc Imaging.* 2008 Jul;1(4):424-33. PubMed Central PMCID: PMC2982260.

- d. Peterson LR, Soto PF, Herrero P, Schechtman KB, Dence C, Gropler RJ. Sex differences in myocardial oxygen and glucose metabolism. *J Nucl Cardiol*. 2007 Jul;14(4):573-81. PubMed Central PMCID: PMC2034520.
4. Through clinical interventional trials, my group has shown salutary effects of inorganic nitrate on exercise performance in patients with heart failure with reduced ejection fraction and others.
 - a. Coggan AR, Broadstreet SR, Mahmood K, Mikhalkova D, Madigan M, Bole I, Park S, Leibowitz JL, Kadkhodayan A, Thomas DP, Thies D, Peterson LR. Dietary Nitrate Increases VO_2 peak and Performance but Does Not Alter Ventilation or Efficiency in Patients With Heart Failure With Reduced Ejection Fraction. *J Card Fail*. 2018 Feb;24(2):65-73. PubMed Central PMCID: PMC5811385.
 - b. Rimer EG, Peterson LR, Coggan AR, Martin JC. Increase in Maximal Cycling Power With Acute Dietary Nitrate Supplementation. *Int J Sports Physiol Perform*. 2016 Sep;11(6):715-720. PubMed Central PMCID: PMC4889556.
 - c. Coggan AR, Leibowitz JL, Spearie CA, Kadkhodayan A, Thomas DP, Ramamurthy S, Mahmood K, Park S, Waller S, Farmer M, Peterson LR. Acute Dietary Nitrate Intake Improves Muscle Contractile Function in Patients With Heart Failure: A Double-Blind, Placebo-Controlled, Randomized Trial. *Circ Heart Fail*. 2015 Sep;8(5):914-20. PubMed Central PMCID: PMC4573847.
 - d. Coggan AR, Leibowitz JL, Kadkhodayan A, Thomas DP, Ramamurthy S, Spearie CA, Waller S, Farmer M, Peterson LR. Effect of acute dietary nitrate intake on maximal knee extensor speed and power in healthy men and women. *Nitric Oxide*. 2015 Aug 1;48:16-21. PubMed Central PMCID: PMC4362985.