BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
McLaughlin, Tracey L.	Professor, Department of Medicine, Division of Endocrinology
eRA COMMONS USER NAME (credential, e.g., agency login) MCLAUGHLIN.TRACEY	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Stanford University, Stanford, CA	B.A.	1988	Human Biology
Univ. CA, Berkeley, Berkeley, CA	M.S.	1992	Med/Public Health
Univ. CA, San Francisco, San Francisco, CA	M.D.	1994	Medicine
Stanford University, Stanford, CA	M.S	2004	Epidemiology

A. Personal Statement

My research centers on the relationship between obesity and insulin resistance. Not all overweight/ obese individuals are insulin resistant, and those who are have a substantially increased risk for diabetes, cardiovascular disease, and malignancy. Clinical metabolic studies conducted in my laboratory include weight loss studies, in which dietary and surgical interventions are evaluated with respect to metabolic changes, and weight gain studies, in which controlled calorie excess is used to induce a variable degree of insulin resistance. In addition to our expertise in designing diet studies, we are equipped to perform a wide variety of quantitative metabolic studies to assess insulin action and beta cell function. Furthermore, we perform adipose tissue biopsies, separate adipose from stromal-vascular cells, grow preadipocytes in culture, and perform various analyses on the cells and/or tissue including adipose cell size distribution, immunohistochemistry, flow cytometry, and gene and protein expression to evaluate adipose, immune cells, and extracellular matrix components in human fat. Relationships with our bariatric and cardiac surgeons allow us to study visceral and epicardial fat as well. We are adept in utilizing various radiologic methods to quantify regional, intrahepatic, and intra myocellular fat deposition, so changes in fat depots can be related to changes in metabolism and/or adipose cell indices. More recently, the addition of deep omics profiling of blood and adipose tissue has added a new method by which we can examine pathways linking obesity to insulin resistance. These tools are used to address an overarching hypothesis that dysfunctional adipose cells and aberrant matrix/immune responses to adipocyte stress underlie human insulin resistance. As a clinical investigator, I maintain active collaborations with many basic scientists at Stanford and embrace a team-science approach that yields innovative translational projects.

a. **McLaughlin T**, Lamendola C, Coghlan N, Liu TC, Lerner K, Sherman A, Cushman SW. Subcutaneous Adipose Cell Size and Distribution: Relationship to Insulin Resistance and Body Fat. Obesity 2014, 22:673.
b. **McLaughlin T**, Liu LF, Lamendola C, Engleman E. T-Cell Profile in Adipose Tissue is Associated with Insulin Resistance and Systemic Inflammation in Humans. ATVB 2014, 34:2637-43.
c. Liu LF, Kodama K, Wei K, Tolentino LL, Choi O, Engleman EG, Butte AJ, **McLaughlin T**. The receptor CD44 is associated with systemic insulin resistance and proinflammatory macrophages in human adipose tissue. Diabetologia 2015, 58:1579-86.
d. **McLaughlin T**, Craig C, Liu LF, Perelman D, Allister C, Spielman D, Cushman SW. Adipose Cell Size and Regional Fat Deposition as Predictors of Metabolic Response to Overfeeding in Insulin-Resistant and Insulin-Sensitive Humans. Diabetes 2016 epub Feb 16.
e. Piening B, Zhou W, Contrepois K, Rost H, Gu G, Mishra T, Hansen B, Bautista E, Leopold S, Yeh C, Spakowicz D, Kukurba K, Perelman D, Craig C, Colbert E, Salins D, Rego S, Wheeler J, Abbott C, Pitteri S, Sodergren E, **McLaughlin T***, Weinstock G*, and Michael Snyder*. Integrative Personal Omics Profiles During Periods of Weight Gain and Loss. Cell Systems 2017, 6:157-170.
f. Zhou W, Sailani R, Contrepois K, Zhou Y, Ahadi S, Leopold S, Zhang MJ, RaoV, Avina M, Mishra T, Johnson J, Lee B, Chen S, Tran DB, Nguyen N, Zhou X, Albright B, Hong BY, Petersen L, Bautista E, Hanson B, Spakowicz D, Salins D, Leopold B, Ashland M, Rego S, Limcaoco P, Colbert E, Allister C, Perelman D, Craig C, Miryam S, Rose, SF, Rost H, Tse D, **McLaughlin T**, Sodergren E, Weinstock GM, Snyder M. Longitudinal multi-omics of host-microbe dynamics in prediabetes. Nature 2019, 569(7758):663-671

B. Positions and Honors

Professional Experience:

1988-89	Research Assistant, Cetus Corporation, Dept of Immunology, Emeryville, CA
1994-97	Internship and Residency, Santa Clara Valley Medical Center (county hospital affiliated with Stanford University), San Jose, CA
1997-2000	Fellow in Endocrinology, Stanford University, Stanford, CA
2000-2001	Clinical Instructor and Clinical Research Associate, Stanford University, Department of Medicine, Division of Endocrinology
2002-	Clinical Instructor and Senior Clinical Research Associate, Stanford University, Department of Medicine, Division of Endocrinology
2005-	Assistant Professor, Stanford University, Department of Medicine, Division of Endocrinology
2012-	Associate Professor, Stanford University, Department of Medicine, Division of Endocrinology
2017-	Professor, Stanford University, Department of Medicine, Division of Endocrinology

Other Experience and Professional Memberships

1997-	American Diabetes Association, Nutrition and Metabolism Section
2000-	Endocrine Society
1997,2002-3	American Association of Clinical Endocrinologists
2002	Consensus Committee, AACE/ACE, for Insulin Resistance Syndrome, Washington D.C.
2002-	GCRC Advisory Committee, voting member, Stanford University
1997-	Teaching Assistant for "Human Physiology", Stanford University School of Medicine
2002-3	Teaching Assistant for "Clinical Investigation", Stanford University School of Medicine
2003-6	Scholarly Concentration in Women's Health and Comparative Medicine and Biology, Mentor
2005-12	Founder and Chair of Diabetes Task Force, Stanford University
2007-2010	Co-Chair of the Bay Area Diabetes Club
2007-2020	Word Congress on Insulin Resistance, Steering Committee Member
2009-12	Endocrine Society, Special Programs Committee Member
2010	Scientific Review Panel, Metabolic Dysfunction Collaborative, NIDDK, NIH
2012-13	American Diabetes Association, Steering Committee Member
2014, 2017-20	Scientific Review Panel, CIDO, NIDDK, NIH
2014-	American Diabetes Association, Abstract Reviewer
2015-	American Diabetes Association, Grant Reviewer

Honors

1989	B.A. granted with honors and distinction, Stanford University
1992	The Secretary's Award for Innovations in Health and Human Services, US Department of Health and Human Services
1995	Intern of the Year, Santa Clara Valley Medical Center
1997	Winner of Associated Research Poster Competition, American College of Physicians, Philadelphia, PA
1998	Endocrine Fellows Foundation Research Award
2000	K23 Clinical Research Award
2004	American Federation for Medical Research, Junior Investigator Award
2009	Mentor to Recipient of Endocrine Fellows Foundation Award
2013	Mentor to Recipient of Stanford TRAM Award
2014	Mentor to Recipient of Stanford TRAM Award
2015	SPARK Award, Stanford University
2018	PHIND Dream Team Award, Stanford University

C. Contributions to Science

1. My early research addressed the hypothesis that that not all overweight/obese individuals are insulin resistant (IR), and that metabolic and cardiovascular risk is concentrated in the IR subgroup. I performed a number of studies utilizing a study design in which BMI-matched overweight/obese individuals, classified as either insulin resistant or insulin sensitive using the modified insulin-suppression test (developed by my mentor, Gerald Reaven), were compared. These studies led to multiple publications showing that IR as compared to BMI-matched IS individuals demonstrated hypertension, hypertriglyceridemia, low HDL-cholesterol, higher plasma glucose, systemic inflammation, hypercoagulability, endothelial dysfunction, postprandial lipemia, higher daylong insulin and leptin concentrations, and lower adiponectin concentrations. I not only demonstrated that the IR subgroup of overweight/obese is at higher risk than the IS subgroup, but that dietary weight loss leads to improvement in risk

factors in the IR, but not the IS subgroup. Thus, my research contributed to the emerging concept that while obesity and insulin resistance are associated, they are not synonymous, and that it is important to identify the IR subset of overweight/moderately-obese individuals who are at excess risk for clinical disease, and who experience risk reduction with modest weight loss.

a. **McLaughlin T**, Abbasi F, Lamendola C, Liang L, Reaven G, Schaaf P, Reaven P. Differentiation between obesity and insulin resistance in the association with c-reactive protein. Circulation 2002; 106: 2908-2912.
b. **McLaughlin T**; Abbasi F; Kim HS; Lamendola C; Schaaf P; Reaven G. Relationship between insulin resistance, weight loss and coronary heart disease risk in obese healthy women. Metabolism 2001; 50:795-800.
c. **McLaughlin T**, Stuhlinger M, Lamendola C, Abbasi F, Reaven GM, Tsao PS. Plasma Asymmetric dimethylarginine concentrations are elevated in insulin-resistant women and fall with weight loss. J Clin Endocrinol Metab 2006; 91:1896-900.
d. **McLaughlin T**, Abbasi F, Lamendola C, Reaven G. Heterogeneity in prevalence of risk factors for cardiovascular disease and type 2 diabetes in obese individuals: impact of differences in insulin sensitivity. Archives Int Med. 2007; 167:642-8.

2. My second major contribution to science was identifying biomarkers by which to identify the high-risk overweight/obese individual. Because insulin resistance can only be measured in a research laboratory and the majority of surrogate markers (eg HOMA) require an insulin concentration, which is not standardized across clinical laboratories, I published several papers that demonstrated the utility of fasting plasma triglyceride and triglyceride-to-HDL-cholesterol ratio as biomarkers for insulin resistance. These are now widely used not only in research, but also in clinical practice and are listed in standard clinician resources such as Up-to-Date®.

a. **McLaughlin T**, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann of Intl Med 2003; 139:802-809.
b. **McLaughlin T**, Reaven G, Abbasi F, Lamendola C, Krauss R. Is there a simple way to identify insulin-resistant individuals at increased risk of cardiovascular disease? Am J Cardiol 2005, 96:399-404.
c. Reaven G, **McLaughlin T**. Why the plasma triglyceride/high-density lipoprotein cholesterol concentration ratio does not predict insulin resistance in African Americans. Archives of Internal Medicine 2006;166:249-50.

3. Following the early studies were a number of studies evaluating the impact of dietary macronutrient composition on metabolic risk factors. Of particular interest, and the subject of my NIH-K-award, was the notion that because high-carbohydrate diets stimulate insulin secretion, particularly in IR subjects, weight loss may be attenuated and metabolic benefits of weight loss mitigated as compared to similar weight loss with a low-carbohydrate diet. Publications, listed below, contributed to the currently accepted view that weight loss is a function of calorie balance and compliance with diet, but macronutrient composition has differential effects on metabolic risk factors, which appear to be reduced to a greater degree on the lower carbohydrate diets.

a. **McLaughlin T**; Abbasi F; Lamendola C; Yeni-Komshian H; Reaven G. Carbohydrate-induced hypertriglyceridemia: an insight into the link between plasma insulin and triglyceride concentrations. J Clin Endocrinol Metab 2000; 85(9):3085-3088.
b. **McLaughlin T**, Carter S, Abbasi F, Lamendola C, Schaaf P, Yee G, Reaven G. Moderate variations in carbohydrate and fat content of hypocaloric diets: impact on weight loss, insulin resistance, and cardiovascular risk in insulin-resistant, obese individuals. Am J Clin Nutr 2006; 84:813-21.
c. Ryan, M, Abbasi F, Lamendola C, Carter S, **McLaughlin T**. Serum alanine aminotransferase levels decrease further with carbohydrate than fat restriction in insulin-resistant adults. Diabetes Care. 2007; 30:1075-80.
d. **McLaughlin T**, Carter S, Abbasi F, Lamendola C, Schaaf P, Basina M, Reaven G. Clinical efficacy of two calorie-restricted diets in overweight patients with type2 diabetes not receiving pharmacological agents: comparison of moderate fat versus carbohydrate reductions. Diabetes Care. 2007;30:1877-9.

4. Based on the observation that obesity is not synonymous with metabolic disease, the last decade has been devoted to examination of the biological characteristics of adipose tissue that characterize the insulin resistant state. These studies include cross-sectional comparisons of BMI-matched insulin-resistant vs sensitive individuals, as well as pre vs post weight perturbation (diet, medication, or surgical weight loss and overfeeding/experimental weight gain). With Samuel Cushman (NIH), we demonstrated that all individuals have both large and small adipose cells, and that with expanding body mass, the increase in adipose cell size diameter is insufficient to accommodate the excess fat mass, thus implicating increase in adipose cell number as a necessary response to weight gain/obesity. In addition, we demonstrated that not only is insulin resistance associated with hypertrophy of large adipose cells, but also with accumulation of small adipose cells. The novel latter observation extended findings in mice, and has contributed to

the current thinking that adipose cell number in humans is not fixed after adolescence as once believed, but that an increase in adipose cell number is necessary to accommodate excess body fat in human obesity. In addition, with Edgar Engleman (Stanford) we demonstrated that inflammation in subcutaneous fat is associated with insulin resistance independent of BMI, that subpopulations of immune cells are related to insulin resistance, including Th1 and 2 and CD44+macrophages, and that presence of proinflammatory macrophages impairs differentiation of human preadipocytes. We are now exploring inflammation during weight gain and loss with flow cytometry, advanced multi-omics, as well as functional assays of immune cell activity and phenotype in blood and adipose tissue.

a. **McLaughlin T**, Sherman A, Tsao P, Gonzalez O, Yee G, Lamendola C, Reaven GM, Cushman SW. Enhanced proportion of small adipose cells in insulin-resistant versus insulin-sensitive individuals implicates impaired adipogenesis. Diabetologia. 2007; 50:1707-15.
b. **McLaughlin T**, Deng A, Gonzales O, Aillaud M, Yee, G, Lamendola C, Abbasi F, Connoly A, Sherman A, Cushman C, Reaven GM, Tsao P. Comparison of Inflammatory Markers in Subcutaneous Adipose Tissue Obtained from Equally Obese Insulin Resistant and Insulin Sensitive Women. Diabetologia, 2008; 51:2303-8.
c. **McLaughlin T**, Liu T, Yee G, Abbasi F, Lamendola C, Reaven G, Tsao P, Cushman SW, Sherman A. Pioglitazone Increases the Proportion of Small Cells in Human Subcutaneous Adipose Tissue. Obesity 2010, 18:926-31.
d. **McLaughlin T**, Lamendola C, Liu A, Abbasi F. Subcutaneous and Visceral Fat Depots: Bidirectional Relationship with Insulin Resistance. J Clin Endocrinol Metab 2011, 96:E1756-60.
e. Winer DA, Winer S, **McLaughlin T**, Miklos D, Dosch HM, Engleman EG. B Lymphocytes Promote Insulin Resistance through Modulation of T Lymphocytes and Production of Pathogenic IgG Antibody. Nat Med 2011, 17:610-7.

Complete List of Published Work in MyBibliography:
https://www-ncbi-nlm-nih-gov.laneproxy.stanford.edu/myncbi/tracey.mclaughlin.1/bibliography/public/

D. Research Support

Ongoing Research Support

NIH/NIDDK 1 R01 DK110186-01A1 McLaughlin (PI) 04/01/2017 - 03/31/2022
Longitudinal multi-omic profiles to reveal mechanisms of obesity-mediated insulin resistance
The goals of this project include studying mechanisms of obesity-induced insulin resistance using a controlled weight perturbation intervention and omics methods in overweight humans

American Diabetes Association 1-19-ICTS-073 McLaughlin (PI) 07/01/2019 - 06/30/2022
Role of altered nutrient transit and incretin hormones in glucose lowering after Roux-en-Y gastric bypass surgery
The goal of this project is to extend current knowledge regarding the pathophysiology of glucose lowering following RYGB, particularly in the case of postbariatric hypoglycemia

NIH/NHLBK 1R01HL14669001 Wu (PI) 04/01/2019 – 3/31/2023
Genetic and Stem Cell Model of Cardiac Metabolic Disease
Major Goals: Gain insight into the clinical relevance of in vitro phenotypic characterization of iPSC-derived cardiomyocytes and endothelial cells with respect to type 2 diabetes.

Merck Co SPO 154001 McLaughlin (PI) 12/19/2019 – 12/18/2022
Ertugliflozin: Cardioprotective Effects on Epicardial Fat
Major Goals: Determine the effect of ertugliflozin on epicardial fat including fat storage, lipolysis, and inflammation.

PHIND at Stanford University McLaughlin (Co-PI) 10/15/17 – 3/15/20 (no-cost extension)
Precision Diets for Diabetes Prevention
In this study we will metabolically profile individuals with prediabetes and through machine learning will identify the best diet for metabolic health.

Completed Research Support

Takeda Pharmaceuticals McLaughlin (Co-PI) 04/06/05 – 04/05/07
Role of Adipocytes in Insulin Resistance and Cardiovascular Disease Risk: Modulation With Pioglitazone
Determine the role of the adipocyte in the development of insulin resistance and cardiovascular disease.

NIH/NIDDK 5 R01DK071309 Reaven (PI) 05/01/05-04/30/09
Integrating the Metabolic and Genetic Faces of Obesity
Explore the hypothesis that impaired adipocyte differentiation and subcutaneous fat storage plays a role in insulin resistance. Insulin resistant and insulin sensitive obese subjects were randomized to pioglitazone or weight loss.
Role: Co-Investigator, Study Director

Eli Lilly and Company McLaughlin (PI) 12/20/07-06/30/13
RCT Investigating Exenatide for Diabetes Prevention in Obese, Insulin-resistant Individuals with Prediabetes:
Investigate whether use of exenatide and caloric restriction, versus caloric restriction alone, in prediabetic individuals can restore both first phase insulin response and improve insulin sensitivity, in essence, reversing the prediabetic phenotype.

NIH/NIDDK R01 DK080436 McLaughlin (PI) 07/01/09-12/31/13
Heterogeneity of Fat Depots:
Ascertain biologic properties of adipose tissue (differentiation, fat storate, ectopic fat, inflammation) from different depots that relate to insulin resistance.

ADA 1-11-CT35 McLaughlin (PI) 01/01/11– 12/31/13
Adipose Tissue Response to Overfeeding in Insulin Resistance-prone vs Insulin-sensitive Humans:
Compare response of adipose cells and tissue to overfeeding in humans who are insulin sensitive vs insulin resistant in order to ascertain the healthy vs maladaptive responses to calorie excess that may contribute to insulin resistance.

Nutrition Science Initiative (NuSI) Gardner (PI) 09/01/13 - 08/31/16
Diet X Genotype
The goal of this large study (n=600), supported in part by NIH, is to determine whether genotype interacts with dietary macronutrient composition in metabolic and adipocyte response to hypocaloric diet.
Role (Co-Investigator, Director of Adipose Biopsy Component)

ADA Translational Research Award McLaughlin (PI) 1/1/14-12/31/17
Adaptive Immune Response: Role in Human Insulin Resistance
The goal of this research is to test the hypothesis that the balance of pro and anti-inflammatory T cells in adipose tissue is related to insulin sensitivity and macrophage phenotype, before and after experimentally-induced weight gain.

NIH 1U54DE02378901 Snyder (PI) 9/06/13- 12/31/17
Longitudinal Multiomics Microbial Profiling in Healthy and Disease Individuals
Profile prediabetic longitudinally to identify biomarkers and microbiome that predict conversion to type 2 diabetes.
Role (Co-Investigator)

American Heart Association, California Affiliate 17GRNT33460003 McLaughlin (PI) 01/01/2017 - 12/31/2018
Adaptive Immune Response in Visceral and Subcutaneous Fat: Role in Human Insulin Resistance

NIH/NIDDK 2 R01 DK081371-06 Palaniappan (PI) 9/1/2014 – 3/31/2019
Strength Training Regimen for Normal-weight Diabetics (STRONG-D)
This study seeks to determine whether strength training, aerobic training, or combined strength and aerobic training, is most effective, compared to no exercise, in treating normal-weight individuals with type 2 diabetes.
Role (Co-Investigator)

Cardiometabolic Disease Research Foundation McLaughlin (PI) 10/01/2016 - 12/31/2019
Human Epicardial Fat and Coronary Atherosclerosis Adjacent to the Myocardial Bridge
The major goal is to test the hypothesis that human epicardial adipose tissue contributes to underlying CAD by outside-to-inside molecular and cellular signaling via inflammatory pathways

Novo Nordisk, IIT McLaughlin (PI) 09/01/14 - 12/31/19
Effect of Liraglutide on Macrophage Polarization in Human Adipose Tissue and Peripheral Blood
The goal of this study is to determine whether liraglutide causes M2 polarization in human adipose tissue and blood in obese type 2 diabetics.