BIOGRAPHICAL SKETCH

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NAME: Mark O. Goodarzi, M.D., Ph.D.

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

POSITION TITLE: Professor of Medicine; Director, Division of Endocrinology, Diabetes and Metabolism

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Harvard University	B.A.	05/1993	Biochemistry
University of California San Francisco	M.D.	06/1997	
University of California Los Angeles Medical Center		06/1999	Residency in Internal Medicine
University of California Los Angeles Medical Center		06/2004	Fellowship in Endocrinology
University of California Los Angeles	Ph.D.	06/2004	Human Genetics

A. Personal Statement:

I am the Director of the Division of Endocrinology, Diabetes and Metabolism, of the Department of Medicine at Cedars-Sinai Medical Center (CSMC) and Professor of Medicine at CSMC and at the David Geffen School of Medicine at the University of California Los Angeles. I also hold the Eris M. Field Endowed Chair in Diabetes Research at CSMC. I am both a diabetologist-endocrinologist and a molecular geneticist, and head of the Endocrine Genetics Laboratory at CSMC. For over a decade, my research has included molecular biologic, genetic epidemiologic, epigenetic, and clinical investigations in multiple ethnic groups, particularly Hispanic and non-Hispanic Caucasians. I have conducted extensive studies of the molecular genetics of insulin resistance and insulin metabolism and related cardiovascular traits, and published the first report describing the high heritability of insulin clearance. I currently serve as multi-PI on the R01 “Improving beta-cell function in Mexican American women with prediabetes,” the R01 “Impact of the gut microbiome and diet on change in insulin homeostasis and cardiometabolic risk,” (MILES, Microbiome and Insulin Longitudinal Evaluation Study) and the U01 “Pathophysiology, epidemiology, and prevention of pancreatogenic diabetes.” I also lead the research program in polycystic ovary syndrome (PCOS) genetics at CSMC. I have also been involved in physiologic phenotyping of insulin-related traits; my team established the insulin suppression test (IST) at CSMC. I am the co-convener (with James Meigs) of the CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) Glycemia-Diabetes Working Group, an international consortium that assembled over 20 cohorts (comprising over 100,000 individuals) for the study of common and rare variants that contribute to glucose homeostasis and type 2 diabetes. In these research activities, as well as in my role as Division Director, I serve as a mentor to post-doctoral fellows and junior faculty and am heavily involved in coordinating clinical and research training activities. The manuscripts listed below are evidence of my ability to integrate human genetics into multidisciplinary research (a) and lead multicenter consortium studies (b).

a. Song Y, Altarejos J, **Goodarzi MO**, Inoue H, Guo X, Berdeaux R, Kim J-H, Goode J, Igata M, Paz J, Hogan MF, Singh P, Goebel N, Vera L, Miller N, Cui J, Jones MR, CHARGE Consortium, GIANT Consortium, Chen YDI, Taylor KD, Hsueh WA, Rotter JI, Montminy M. CRTC3 links catecholamine signaling to energy balance. Nature 2010;468:933-9. PMCID: PMC3025711
b. Wessel J, Chu AY, Willems SM, Wang S, et al., Rotter JI, Meigs JB, Scott RA, **Goodarzi MO**. Low-frequency and rare exome chip variants associate with fasting glucose and type 2 diabetes susceptibility. Nat Commun 2015;6:5897. NIHMSID: 642453

B. Positions and Honors

Positions and Employment

2004-present	Staff Physician, Division of Endocrinology, Diabetes and Metabolism; Medical Genetics Research Institute, Cedars-Sinai Medical Center
2005-2010	Assistant Professor of Medicine, David Geffen School of Medicine at UCLA
2007-2010	Associate Director, Division of Endocrinology, Diabetes & Metabolism, Cedars-Sinai
2008-2014	Site Director, Endocrinology Fellowship Program, Cedars-Sinai Medical Center
2010-2013	Associate Professor of Medicine, Cedars-Sinai Medical Center
2010-2014	Associate Professor of Medicine, David Geffen School of Medicine at UCLA
2010-present	Director, Division of Endocrinology, Diabetes & Metabolism, Cedars-Sinai
2014-present	Professor of Medicine, Cedars-Sinai Medical Center
2014-present	Professor of Medicine, David Geffen School of Medicine at UCLA

Other Experience and Professional Memberships

1998-present	American College of Physicians, Member
1999-present	Endocrine Society, Member
2000-present	American Association of Clinical Endocrinologists, Member
2002-present	Ad hoc reviewer, *Fertil Steril*, *Metabolism*
2003-present	American Heart Association, Member; American Society of Human Genetics, Member
2004-present	American Diabetes Association, Member; Androgen Excess and PCOS Society, Member
2004-present	Editorial Consultant, *Physicians' Information and Education Resource (PIER)*
2004-present	Ad hoc reviewer, *Diabetologia, J Clin Endocrinol Metab*
2005-present	Ad hoc reviewer, *J Lipid Res, Genet Med, Clin Endocrinol, Eur Heart J*
2006-present	Ad hoc reviewer, *Hum Reprod*, *Diabetes*, *Circulation*, *Ann Intern Med, Atherosclerosis*
2006-present	American Federation of Medical Research, Member
2007 October	Ad hoc member, Clinical and Integrative Cardiovascular Sciences Study Section, NIH
2009-present	Ad hoc reviewer, *Mol Cell Endocrinol, Mol Hum Reprod, Gynecol Endocrinol*
2009 June	Ad hoc member, Special Emphasis Panel, Challenge Grants Panel 19, NIH
2010 April	Chairman and ad hoc member, Special Emphasis Panel, ZDK1 GRB-N (M6), NIH
2010 June	Ad hoc member, Kidney, Nutrition, Obesity and Diabetes (KNOD) Study Section, NIH
2010 September	Ad hoc member, Special Emphasis Panel, ZDK1 GRB-B (O1), NIH
2011 May	Ad hoc member, Population Sciences and Epidemiology (PSE) Study Section, NIH
2011-present	Ad hoc reviewer, *Obesity, Horm Metab Res, J Mol Med*
2012-2018	Editorial Board, *Journal of Clinical Endocrinology and Metabolism*
2012-present	Ad hoc reviewer, *PLoS ONE, Trends in Molecular Medicine*
2012 March	Ad hoc member, Special Emphasis Panel, ZRG1 PSE-M (03) M, NIH
2013-2018	Editorial Board, *Fertility and Sterility*
2013 September	Ad hoc member, Special Emphasis Panel, ZDK1 GRB-N (J4), NIH
2014 June	Ad hoc member, Special Emphasis Panel, ZDK1 GRB-N (O3), NIH
2015 June	Ad hoc member, Special Emphasis Panel, ZDK1 GRB-6 (O4), NIH
2016 March	Ad hoc member, Special Emphasis Panel, ZDK1 GRB-J (M1), NIH
2017 March	Ad hoc member, Special Emphasis Panel, ZRG1 PSE-D (02), NIH
2017 June	Ad hoc member, Special Emphasis Panel, ZRG1 DKUS-H (54), NIH
2017 December	Ad hoc member, Special Emphasis Panel, EPID 1, VA Merit Grant Program
2018 March	Ad hoc member, Special Emphasis Panel, ZRG1 CVRS-K (02), NIH
2018 November	Ad Hoc Member, Special Emphasis Panel, ZDK1 GRB-2 (J3), NIH

Honors

1993, 1994	UCSF Student Research Committee Summer Fellowship
1994	Finalist, UCSF Dean's Prize in Research
2000, 2001	Fellow's Outstanding Teacher Award
2002	Awardee, Poster Competition, ACP-ASIM So. California Regions I & II Scientific Session
2002	Finalist, Elizabeth Barrett-Connor Research Award in Epidemiology and Prevention for Young Investigators, Scientific Sessions of the American Heart Association
2003	Pfizer Scholars in Endocrinology Award
2003	UCLA Solomon Scholars Research Award

2004	Finalist, Jeremiah and Rose Stamler Research Award for New Investigators, American Heart Association Conference on Cardiovascular Disease Epidemiology and Prevention
2006	Endocrine Society Travel Grant Award
2006, 2007	Androgen Excess and PCOS Society Young Investigator Award
2008	Western Section, American Federation for Medical Research Outstanding Investigator Award
2008	Cedars-Sinai Winnick Clinical Scholars Award
2009	Western Society for Clinical Investigation Travel Award
2010	Endocrine Society Richard E. Weitzman Memorial Award
2014	Golden Tiger Award for Working Group Leadership, CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) Consortium
2016	*Fertility and Sterility* Star Reviewer Award

C. Contribution to Science

Genetic Basis of Insulin Clearance

I was among the first to report that insulin clearance is a highly heritable trait in Hispanics, with a heritability exceeding those of fasting insulin, insulin resistance, and insulin secretion. I used this work to establish an independent line of NIH-funded research (as PI of R01 DK079888, 1/10/08 to 11/30/13) to search for insulin clearance genes in Hispanics, a group at high risk for diabetes. I identified regions on chromosomes 15 and 20 that harbor genes for insulin clearance in two independent Hispanic cohorts. To directly interrogate the relevance of insulin clearance inheritance to diabetes, obesity and cardiovascular disease, my laboratory used the MetaboChip to find that several of ~50 genes previously identified as diabetes, fasting glucose, and fasting insulin susceptibility loci were found to modulate insulin clearance. I authored the GUARDIAN (Genetics UndeRlying Diabetes in HispaNics) consortium's first paper, which described the genetic architecture of insulin clearance and its genetic and environmental correlations with insulin sensitivity, insulin secretion, and adiposity. These genetic studies may improve our understanding of how the body clears insulin, leading to improved prevention and therapy of diabetes, as well as of other hyperinsulinemic disorders, such as polycystic ovary syndrome.

a. **Goodarzi MO**, Taylor KD, Guo X, Quiñones MJ, Cui J, Li X, Hang T, Yang H, Holmes E, Hsueh WA, Olefsky J, Rotter JI. Variation in the gene for muscle-specific adenosine monophosphate deaminase is associated with insulin clearance, a highly heritable trait. Diabetes 2005;54:1222-7.
b. Guo X, Cui J, Jones MR, Haritunians T, Xiang AH, Chen YD, Taylor KD, Buchanan TA, Davis RC, Hsueh WA, Raffel LJ, Rotter JI, **Goodarzi MO**. Insulin clearance: confirmation as a highly heritable trait, and genome-wide linkage analysis. Diabetologia 2012;55:2183-92. PMCID: PMC3391346
c. **Goodarzi MO**, Guo X, Cui J, Jones MR, Haritunians T, Xiang AH, Chen YDI, Taylor KD, Buchanan TA, Hsueh WA, Raffel LJ, Rotter JI. Systematic evaluation of validated type 2 diabetes and glycemic trait loci for association with insulin clearance. Diabetologia 2013;56:1282-90. PMCID: PMC3651757
d. **Goodarzi MO**, Langefeld CD, Xiang AH, Chen YDI, Guo X, Hanley AJG, Raffel LJ, Kandeel F, Nadler JL, Buchanan TA, Norris JM, Fingerlin TE, Lorenzo C, Rewers MJ, Haffner SM, Bowden DW, Rich SS, Bergman RN, Rotter JI, Watanabe RM, Wagenknecht LE. Insulin sensitivity and insulin clearance are heritable and have strong genetic correlation in Mexican Americans. Obesity 2014;22:1157-64. PMCID: PMC3968231

Physiologic Significance of Insulin Clearance

We found that fasting insulin, used by many as a surrogate for insulin resistance, is actually more highly influenced by insulin clearance; this critical result has major implications for large scale epidemiologic studies that rely on fasting insulin. We found that insulin clearance is positively correlated with insulin sensitivity and negatively correlated with insulin secretion and adiposity. Differences in insulin clearance by race/ethnicity (lower in African Americans and Hispanics compared with non-Hispanic whites) were largely explained by differences in adiposity, insulin sensitivity, and insulin secretion. We discovered that low insulin clearance is a predictor of incident diabetes that developed over five years of follow-up in Hispanic and African-American families (Insulin Resistance Atherosclerosis (IRAS) Family Study), highlighting the crucial need to better understand this trait. We discovered novel associations of hepatic lipase and apolipoprotein A-I with insulin clearance. Identification of metabolic traits that influence insulin clearance complements my search for genetic traits that influence insulin clearance.

a. **Goodarzi MO**, Cui J, Chen YDI, Hsueh WA, Guo X, Rotter JI. Fasting insulin reflects heterogeneous physiologic processes: role of insulin clearance. Am J Physiol Endocrinol Metab 2011;301;E402-8. PMCID: PMC3154529.

b. Lorenzo C, Hanley AJG, Wagenknecht LE, Rewers MJ, Stefanovski D, **Goodarzi MO**, Haffner SM. Relationship of insulin sensitivity, insulin secretion, and adiposity to insulin clearance in a multiethnic population: The Insulin Resistance Atherosclerosis Study. Diabetes Care 2013;36:101-3. PMCID: PMC3526225.
c. Lee CC, Haffner SM, Wagenknecht LE, Lorenzo C, Norris JM, Bergman RN, Stefanovski, Anderson AM, Rotter JI, **Goodarzi MO***, Hanley AJG*. Insulin clearance and the incidence of type 2 diabetes in Hispanics and African-Americans: The IRAS Family Study. Diabetes Care 2013;36:901-7. *Equal senior author status. PMCID: PMC3609510
d. Labadzhyan A, Cui J, Péterfy M, Guo X, Chen YI, Hsueh WA, Rotter JI, **Goodarzi MO**. Insulin clearance is associated with hepatic lipase activity and lipid and adiposity traits in Mexican Americans. PLoS One 2016;11:e0166263. PMCID: PMC5112869.

Genetic Studies of Physiologically Measured Glucose Homeostasis Traits

Genome-wide association studies (GWAS) in type 2 diabetes have revealed many loci that influence beta cell function but few that influence insulin sensitivity, in part because insulin sensitivity has not been precisely phenotyped in large cohorts. I have had the privilege of participating in the first large-scale GWAS for insulin resistance measured by physiologic studies (e.g., euglycemic clamp). I lead Cedars-Sinai participation in the GUARDIAN (Genetics UndeRlying Diabetes in HispaNics) study, consortium that has assembled six cohorts (totaling >4000 Hispanic subjects) for a GWAS of insulin clearance and insulin resistance. GUARDIAN recently contributed to the discovery of a novel gene for insulin sensitivity, NAT2.

a. **Goodarzi MO**, Guo X, Taylor KD, Quiñones MJ, Saad MF, Yang H, Hsueh WA, Rotter JI. Lipoprotein lipase is a gene for insulin resistance in Mexican-Americans. Diabetes 2004;53:214-20.
b. Rich SS*, **Goodarzi MO***, Palmer ND, Langefeld CD, Ziegler J, Haffner SM, Bryer-Ash M, Norris JM, Taylor KD, Haritunians T, Rotter JI, Chen YDI, Wagenknecht LE, Bowden DW, Bergman RN. A genome-wide association scan for acute insulin response to glucose in Hispanic Americans: the IRAS Family Study. Diabetologia 2009;52:1326-33. *Equal first author status. PMCID: PMC2793118
c. Knowles JW, Xie W, Zhang Z, Chennemsetty I, Assimes TL, Paananen J, Hansson O, Pankow J, **Goodarzi MO**, Carcamo-Orive I, Morris A, Chen YDI, Mäkinen V, Ganna A, Guo X, Mahajan A, Abbasi F, Greenawalt DM, Lum P, Molony C, Lind L, Lindgren C, Raffel Lj, Tsao P, The RISC Consortium, The EUGENE2 Study, The GUARDIAN Consortium, The SAPPHIRe Study, Schadt EE, Rotter JI, Sinaiko A, Reaven G, Yang X, Hsiung CA, Groop L, Cordell HJ, Laakso M, Hao K, Ingelsson E, Frayling TM, Weedon MN, Walker M, Quertermous T. Genome wide identification and functional validation of *NAT2* as a human insulin sensitivity gene. J Clin Invest 2015;125:1739-51. PMCID: PMC4409020
d. Palmer ND*, **Goodarzi MO***, Langefeld CD*, Wang N*, Guo X, Taylor KD, et al., Chen Y-DI, Bowden DW, Rich SS, Raffel LJ, Rotter JI, Watanabe RM, Wagenknecht LE. Genetic variants associated with quantitative glucose homeostasis traits translate to type 2 diabetes in Mexican Americans: the GUARDIAN (Genetics Underlying Diabetes in Hispanics) Consortium. Diabetes 2015;64:1853-66. PMCID: PMC4407862. *Equal first author status.

Genetic and Molecular Basis of Polycystic Ovary Syndrome

The first two GWAS in polycystic ovary syndrome (PCOS) were conducted in Chinese subjects and identified variants at 11 loci. We examined several of these loci in the form of a genetic risk score, finding association with PCOS in Europeans. We also contributed to PCOS GWAS studies in Europeans. We conducted a systems genetics study that suggests unique molecular mechanisms for PCOS exist in obese women. Identification of susceptibility genes is anticipated to lead to new modalities of managing PCOS.

a. Brower MA, Jones MR, Rotter JI, Krauss RM, Legro RS, Azziz R, **Goodarzi MO**. Further investigation in Europeans of susceptibility variants for polycystic ovary syndrome discovered in genome-wide association studies of Chinese individuals. J Clin Endocrinol Metab 2015;100:E182-6. PMCID: PMC4283012
b. Jones MR, Brower MA, Xu N, Cui J, Mengesha E, Chen YDI, Taylor KD, Azziz R, **Goodarzi MO**. Systems genetics reveals the functional context of PCOS loci and identifies genetic and molecular mechanisms of disease heterogeneity. PLoS Genet 2015;11:e1005455. PMCID: PMC4549292.
c. Hayes MG, Urbanek M, Ehrmann DA, Armstrong LL, Lee JY, Sisk R, Karaderi T, Barber T, McCarthy MI, Franks S, Lindgren CM, Welt CK, Diamanti-Kandarakis E, Panidis D, **Goodarzi MO**, Azziz R, Zhang Y, James RG, Olivier M, Kissebah AH, Reproductive Medicine Network, Stener-Victorin E, Legro RS, Dunaif A. Genomewide association of polycystic ovary syndrome implicates alterations in gonadotropin secretion in European ancestry populations. Nat Commun 2015;6:7502. PMCID: PMC4557132

d. Day F, Karaderi T, Jones MR, …, **Goodarzi MO**, et al. Large-scale genome-wide meta analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnosis criteria. PLoS Genetics. In press.

Interrelationships between Diabetes, Pancreatitis, and Pancreatic Cancer
I co-chair the Type 3c DM Working Group within the NIH-funded Consortium for the Study of Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC). We summarized current understanding and knowledge gaps in pancreatogenic diabetes and how obesity and diabetes affect the risk of PDAC. As even a single episode of acute pancreatitis increases the risk of diabetes, we characterized relationships between insulin, glucagon, and pancreatic polypeptide and digestive enzymes. We published the rationale and design of the DETECT study, which proposes depressed pancreatic polypeptide response after meal stimulation is a biomarker for pancreatogenic diabetes.

a. Hart PA, Bellin MD, Andersen DK, Bradley D, Cruz-Monserrate Z, Forsmark CE, **Goodarzi MO**, et al. Type 3c (pancreatogenic) diabetes mellitus secondary to chronic pancreatitis and pancreatic cancer. Lancet Gastroenterol Hepatol 2016;1:226-37. PMCID: PMC5495015
b. Bharmal SH, Pendharkar SA, Singh RG, **Goodarzi MO**, Pandol SJ, et al. Relationship between circulating levels of pancreatic proteolytic enzymes and pancreatic hormones. Pancreatology 2017;17:876-83.
c. Eibl G, Cruz-Monserrate Z, Korc M, Petrov MS, **Goodarzi MO**, et al. Diabetes Mellitus and Obesity as Risk Factors for Pancreatic Cancer. *J Acad Nutr Diet* 2018;118:555-67. PMCID: PMC5845842.
d. Hart PA, Andersen DK, Mather K, et al., **Goodarzi MO.** Evaluation of a mixed meal test for diagnosis and characterization of pancreatogenic diabetes secondary to pancreatic cancer and chronic pancreatitis: rationale and methodology for the DETECT study from the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer. Pancreas 2018;47:1239-43. PMCID: PMC6195331

Complete List of Published Work
http://www.ncbi.nlm.nih.gov/pubmed?term=Goodarzi%20MO[Author]

D. Research Support

Ongoing Research Support

NIH/NICHD HD 074368 (R01) **(M. Goodarzi, Co-Investigator)** **9/15/13–11/30/18**
Title: Adverse Outcomes of Assisted Reproductive Technologies: Genetics or Epigenetics? (M. Pisarska, PI)
Goal: Examine whether *in vitro* fertilization results in epigenetic changes in CVS and term placental samples.

NIH/NIDDK DK 063491 (P30) **(M. Goodarzi, Co-Investigator)** **5/1/13-4/30/19**
Title: Diabetes Research Center (J. Olefsky, PI)
Goal: Dr. Goodarzi co-directs the Genetics Core and serves as Associate Director of the UCSD/UCLA/Salk/Cedars-Sinai Diabetes Research Center Enrichment Program.

NIH/NIMHD MD007867 (R01) **(M. Goodarzi, Multi Principal Investigator)** **8/1/14-5/31/19**
Title: Improving beta-cell function in Mexican American women with prediabetes
Goal: Conduct a pharmacogenetic study of liraglutide and weight loss in women with prediabetes.

NIH/NIDDK DK108314 (U01) **(M. Goodarzi, Multi Principal Investigator)** **9/28/15-8/31/20**
Title: Pathophysiology, epidemiology, and prevention of pancreatogenic diabetes
Goal: Participate in the Consortium for the Study of Pancreatitis, Diabetes, and Pancreatic Cancer.

NIH/NIDDK DK109588 (R01) **(M. Goodarzi, Multi Principal Investigator)** **4/1/17-3/31/22**
Title: Impact of the gut microbiome and diet on change in insulin homeostasis and cardiometabolic risk
Goal: Examine insulin sensitivity, insulin secretion, and insulin clearance with respect to the gut microbiota, habitual diet, and circulating metabolites in a prospective cohort.

Completed Research Support

NIH-NIDDK DK079888 (R01) **(M. Goodarzi, Principal Investigator)** **1/10/08-11/30/13e**
Title: Insulin clearance: candidate and positional genetic determinants
Goal: Identify genes that determine insulin clearance (as defined by euglycemic clamp) in Mexican Americans.

NIH-NIDDK DK085175 (R01) **(M. Goodarzi, Co-Investigator)** **7/20/10-5/31/15e**
Title: Genetic and Epidemiology predictors of glucose homeostasis in Hispanics (L. Wagenknecht, PI)
Goal: Contribute to a GWAS of 4,200 Hispanics with detailed insulin sensitivity and insulin clearance phenotypes (FSIGT or glucose clamp), and follow-up genotyping in 16,000 Hispanics with and without T2D.