

Richard L. Klein, Ph.D.
Associate Professor of Medicine

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

(if applicable)	INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
	College of the Holy Cross, Worcester, MA	A.B.	1973	Biology
	Univ. Texas at Dallas, Richardson, TX	M.S.	1975	Molecular Biology
	Bowman Gray School of Med., Winston-Salem, NC	Ph.D.	1981	Experim. Pathology

Positions and Honors

1975-1981	Graduate Student in the laboratory of Lawrence L. Rudel, Ph.D. in the Specialized Center of Research (SCOR) in Atherosclerosis at the Bowman Gray School of Medicine, Winston-Salem, North Carolina
1981-1984	Postdoctoral Fellow with Donald B. Zilversmit, Ph.D. in the Division of Nutritional Sciences, Cornell University, Ithaca, New York
1984-1989	Research Associate, Department of Medicine, Division of Endocrinology-Metabolism-Nutrition, Medical University of South Carolina, Charleston, South Carolina
1989-2003	Assistant Professor, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina
1986-Present	Research Health Scientist, Research Service, Department of Veteran Affairs Medical Center, Charleston, South Carolina
2003-Present	Associate Professor, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina

Other Experience and Professional Memberships:

- Full Member of the Society of Sigma Xi
- Member, American Heart Association
- Member, American Diabetes Association

Selected peer-reviewed publications (in chronological order)—Selected from a total of 50

- Klein RL**, Lyons TJ, Lopes-Virella MF: Interaction of very low density lipoproteins isolated from Type 1 (insulin-dependent) diabetic patients with human monocyte-derived macrophages. *Metabolism* 38:1108-1114, 1989
- Klein RL**, Lyons TJ, Lopes-Virella MF: Interaction of very low and low density lipoproteins isolated from Type II (non-insulin dependent) diabetic patients with human monocyte derived macrophages. *Diabetologia* 33:299-205, 1990
- Klein RL**, Lopes-Virella MF: Influence of glycemic control on the interaction of very low- and low density lipoproteins isolated from Type 1 (insulin-dependent) diabetic patients with human monocyte-derived macrophages. *Diabetes* 41:1301-07, 1992
- Klein RL**, Lopes-Virella MF: Metabolism by human endothelial cells of very low density lipoprotein subfractions isolated from Type 1 (insulin-dependent) diabetic patients. *Diabetologia* 36:258-264, 1993
- Knapp RG, Schreiner PJ, Sutherland SE, Keil JE, Gilbert GE, **Klein RL**, Hames C, Tyroler HA. Serum lipoprotein(a) levels in elderly black and white men in the Charleston Heart Study. *Clin Genet* 44:225-31, 1993
- Jokl R, **Klein RL**, Laimins M, Lyons TJ, Lopes-Virella MF, Colwell JA. Platelet plasminogen activator inhibitor 1 in patients with type II diabetes. *Diabetes Care* 17:818-823, 1994
- Klein RL**, Laimins M, Lopes-Virella MF: Isolation, characterization and metabolism of glycosylated and non-glycosylated subfractions of low density lipoproteins. *Diabetes* 44:1093-1098, 1995
- Jokl R, **Klein RL**, Lopes-Virella MF, Colwell JA. Release of platelet plasminogen activator inhibitor 1 in whole blood is increased in patients with Type 2 diabetes. *Diabetes Care*, 18:1150-1155, 1995
- Jenkins AJ, **Klein RL**, Chassereau CN, Hermayer KL, Lopes-Virella MF. LDL from patients with well controlled IDDM is not more susceptible to in vitro oxidation. *Diabetes* 45:762-767, 1996.
- Lopes-Virella MF, **Klein RL**, Virella G. Modification of lipoproteins in diabetes. *Diabetes-Metabolism Reviews* 12:69-90, 1996

- Jenkins* AJ, Argyropoulos* G, **Klein RL**, Lyons TJ, Wagenhorst B, St. Amand J, Marcovina S, Albers JJ, Pritchard PH, Garvey WT. Transmission of two novel mutations in a pedigree with familial lecithin:cholesterol acyltransferase deficiency: structure-function relationships and studies in a compound heterozygous proband. *J Lipid Res* 39:1870-1876, 1998.
- Jenkins AJ, Li W, Gates D, Moller K, Fu M-X, **Klein RL**, Baynes JW, Thorpe SR, Lyons TJ. Pre-enrichment of modified LDL with α -tocopherol mitigates their adverse effects on cultured retinal capillary cells. *Current Eye Research* 19:137-145, 1999.
- Lopes-Virella MF, Koskinen S, Mironova M, **Klein RL**, Horne D, Chassereau CN, Enockson C, Virella G. The preparation of copper-oxidized LDL for the measurement of oxidized LDL antibodies by EIA. *Atherosclerosis*, 152:107-115, 2000
- Jenkins AJ, Velarde V, **Klein RL**, Joyce KC, Phillips KD, Mayfield RK, Lyons TJ, Jaffa AA. Native and modified LDL activate extracellular signal-regulated kinases in mesangial cells. *Diabetes* 49:2160-2169, 2000
- Mironova MA*, **Klein RL***, Virella GT, Lopes-Virella MF. Anti-modified LDL antibodies, LDL-containing immune complexes, and susceptibility of LDL to in vitro oxidation in patients with type 2 diabetes. *Diabetes* 49:1033-1041, 2000 (* Authors contributed equally).
- Jenkins AJ, Thorpe SR, Chassereau CN, Onotaro J, Hermayer KL, Otvos JD, King LP, **Klein RL**. The *In vivo* glycated LDL subfraction is not more susceptible to oxidation than non-glycated LDL in Type 1 diabetic patients. *Diabetes* 50:1111, 2001
- Virella G, Atchley D, Koskinen S, Zheng D, **Klein RL**, Lopes-Virella MF, and the DCCT/EDIC Research Group. Proatherogenic and Proinflammatory Properties of Immune Complexes Prepared with Purified Human oxLDL Antibodies and Human oxLDL. *Clinical Immunology* 105:81-92, 2002
- Jenkins AJ, Lyons TJ, Zheng D, Otvos JD, Lackland DT, McGee D, Garvey WT, **Klein RL**, and The DCCT/EDIC Research Group. Lipoproteins in the DCCT/EDIC cohort: Associations with diabetic nephropathy. *Kidney International* 64:817-828, 2003.
- Jenkins AJ, Lyons TJ, Zheng D, Otvos JD, Lackland DT, McGee D, Garvey WT, **Klein RL**, and The DCCT/EDIC Research Group. Serum lipoproteins in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Intervention and Complications cohort: Associations with gender and glycemia. *Diabetes Care* 26:810-818, 2003
- Garvey WT, Kwon S, Zheng D, Shaughnessy S, Wallace P, Hutto A, Pugh K, Jenkins AJ, **Klein RL**, and Liao Y. The effects of insulin resistance and type 2 diabetes mellitus on lipoprotein subclass particle size and concentration determined by nuclear magnetic resonance (NMR). *Diabetes* 52:1-10, 2003
- Klein RL**, Hunter SJ, Jenkins AJ, Zheng D, Semler AJ, Clore J, Garvey WT, and the DCCT/EDIC Research Group. Fibrinogen is a marker for nephropathy and peripheral vascular disease in type 1 diabetes. Studies of plasma fibrinogen and fibrinogen gene polymorphism in the DCCT/EDIC cohort. *Diabetes Care* 26:1439-1448, 2003
- Jenkins AJ, Garvey WT, **Klein RL**. Lipoprotein abnormalities in type 1 diabetes. *Curr Opin Endo Diab* 10:245-250, 2003
- Liao Y, Kwon S, Shaughnessy S, Wallace P, Hutto A, Jenkins AJ, **Klein RL**, Garvey WT. Critical Evaluation of ATP III Criteria in Identifying Insulin Resistance with Dyslipidemia. *Diabetes Care* 27:978-983, 2004
- Jenkins AJ*, Lyons TJ*, Zheng D, Otvos JD, Lackland D, McGee D, Garvey WT, **Klein RL** and The DCCT/EDIC Research Group. Diabetic retinopathy and serum lipoprotein subclasses in the DCCT/EDIC cohort. (* Authors contributed equally) *J Investig Ophthalmol Vis Sci* 45:910-918, 2004
- Klett EL, Lu K, Kosters A, Vink E, Lee M-H, Altenburg M, Shefer S, Batta AK, Yu H, Chen J, **Klein RL**, Looije N, Oude-Elferink R, Groen AK, Maeda N, Salen G, Patel SB. A mouse model of sitosterolemia: absence of ABCG8/Sterolin-2 results in failure to secrete biliary cholesterol. *BMC Med* 2:5, 2005
- Jenkins AJ, Thorpe SR, Chassereau CN, Onotaro J, Hermayer KL, Otvos JD, King LP, **Klein RL**. The *In vivo* glycated LDL subfraction is not more susceptible to oxidation than non-glycated LDL in Type 1 diabetic patients. *Metabolism* 53:969-976, 2004
- Klein RL**, McHenry MB, Lok KH, Hunter SJ, Le N-A, Jenkins AJ, Zheng D, Semler AJ, Brown WV, Lyons TJ, Garvey WT, DCCT/EDIC Research Group. Apolipoprotein C-III protein concentration and gene polymorphisms in type 1 diabetes: Associations with lipoprotein subclasses. *Metabolism* 53:1295-1303, 2004
- MF Lopes-Virella, G Virella, Deyi Zheng, DH Atchley, TJ Lyons, **RL Klein**, DJ Lackland, WT Garvey and the DCCT/EDIC Research Group. LDL-Containing immune complexes are strongly associated with the
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- presence of macro- and microvascular complications and with markers of endothelial damage and inflammation in patients with Type 1 diabetes. *Diabetologia*, In Press, 2006
- Jenkins AJ, Best JD, **Klein RL**, Lyons TJ. Lipoproteins, glycooxidation, and diabetic angiopathy. *Diab Metab Rev* 20:349-368, 2004
- Jenkins AJ, Rowley KG, Lyons TJ, Best JD, Hill MJ, **Klein RL**. Lipoproteins and diabetic microvascular complications. *Curr Pharmaceutical Design* 10:3395-3418, 2004.
- Kraml PJ, **Klein RL**, Huang Y, Nareika A, Lopes-Virella MF. Iron loading increases cholesterol accumulation and macrophage scavenger receptor-1 expression in THP-1 mononuclear phagocytes. *Metabolism* 54:453-459, 2005
- Klein RL**, McHenry MB, Lok KH, Hunter SJ, Le N-A, Jenkins AJ, Zheng D, Semler AJ, Page G, Brown WV, Lyons TJ, Garvey WT, DCCT/EDIC Research Group. Apolipoprotein C-III protein concentration and gene polymorphisms in type 1 diabetes: Associations with microvascular disease complications in the DCCT/EDIC cohort. *J Diab Complic*, 19:18-25, 2005
- Sohn M, Tan Y, **Klein RL**, Jaffa AA. Evidence for Low-Density Lipoprotein-induced expression of connective tissue growth factor in mesangial cells. *Kidney Int* 67:1286-1296, 2005
- Fu Y, Luo N, **Klein RL**, Garvey WT. Adiponectin promotes adipocyte differentiation, insulin sensitivity, and lipid accumulation: Potential role in auto-regulation of adipocyte metabolism and adipose mass. *J Lipid Res* 46:1369-1379, 2005
- Klein RL**, Semler AJ, Baynes JW, Thorpe SR, Lyons TJ and Jenkins AJ. Glycation does not alter LDL-induced secretion of tissue plasminogen activator and plasminogen activator inhibitor-1 from human aortic endothelial cells. *Ann. NY Acad. Sci.*, 1043:379-389, 2005
- Lara-Castro C, Luo N, Wallace P, **Klein RL**, Garvey WT. Adiponectin multimeric complexes and the metabolic syndrome trait cluster. *Diabetes* 55:249-259, 2006
- Lyons TJ, Jenkins AJ, Zheng D, **Klein RL**, Otvos JD, Yu Y, Lackland DT, McGee D, McHenry MB, Lopes-Virella MF, Garvey WT, and The DCCT/EDIC Research Group. NMR-determined lipoprotein subclass profile in the DCCT/EDIC cohort: associations with carotid intima-medial thickness. *Diabetic Medicine* 23:955-966, 2006
- Sohn M, Tan Y, Wang B, **Klein RL**, Trojanowska M, Jaffa AA. Mechanisms of low-density lipoprotein-induced expression of connective tissue growth factor in human endothelial cells. *Am J Physiol Heart Circ Physiol* 290:H1624-H1634, 2006
- Jenkins AJ, Rothen M, **Klein RL**, Moller K, Eldridge L, Zheng D, Durazo-Arvizu R, McGee D, Lackland D, Thorpe SR, Garvey WT, Lyons TJ, and the DCCT/EDIC Research Group. Cross-sectional associations of C-reactive protein with vascular risk factors and vascular complications in the DCCT/EDIC cohort. *J Diab Complic* 22:153-163, 2008. NIHMS49462
- Lopes-Virella MF, Carter RE, Gilbert GE, **Klein RL**, Jaffa M, Jenkins AJ, Lyons TJ, Garvey WT, Virella G, and the DCCT/EDIC Study Group. Risk factors related to inflammation and endothelial dysfunction in the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Intervention and Complications (EDIC) cohort and their relationship with nephropathy and macrovascular complications. *Diabetes Care* 31:2006-2012, 2008. PMID: PMC1645
- Tian L, Luo N, **Klein RL**, Chung BH, Garvey TJ, Fu Y. Adiponectin reduces lipid accumulation in macrophage foam cells. *Atherosclerosis* 202:152-161, 2009. PMID: PMC2630479
- Brock JWC, Jenkins AJ, Lyons TJ, **Klein RL**, Yim E, Lopes-Virella MF, Carter RE, Thorpe SR, Baynes JW, and the DCCT/EDIC Research Group. A pilot study of methionine sulfoxide content in apoA-I in Type 1 diabetes. *J Lipid Res* 49:847-855, 2008. PMC Journal – In Process
- Lee M-H, **Klein RL**, El Shewy H, Luttrell DK, Luttrell LM. Adiponectin receptors ADIPOR1 and ADIPOR2 activate ERK1/2 through Src/Ras-dependent pathway and stimulate cell growth in HEK293 cells. *Biochemistry* 47(44):11682-11692, 2008. PMC Journal – In Process
- Tsoi LC, Boehnke M, **Klein RL**, Zheng WJ. Evaluation of genome-wide association study results through development of ontology fingerprint. *Bioinformatics* 2009; doi: 10.1093/bioinformatics/btp158
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Research Support

Interactions of Lipoproteins and Cells in Diabetes Mellitus

3/1/07-2/28/11

Role: Principal Investigator

Funding Agency: Department of Veterans Affairs

The major goals of this project are to define the mechanisms of whereby VLDL decrease adiponectin receptor expression in human endothelial cells.

Biomarkers of Vascular Disease Progression in Diabetes (MF Lopes-Virella, PI)

9/1/08-8/31/13

Role in Project: Co-Investigator

Funding Agency: NIH

The overall objective of this proposal is to assess longitudinally and using repeated measures, biomarkers of endothelial damage, inflammation, and abnormalities of the clotting/fibrinolytic system. We will determine which of these biomarkers or combination of biomarkers will predict the development and/or progression of retinopathy, nephropathy, cardiovascular or peripheral vascular disease. Once the risk panel is established for each complication, we will test it in the remaining patients of the DCCT/EDIC cohort by screening the samples collected in these patients at entry into the DCCT study. That will allow us to determine whether the risk panel developed will accurately predict the development of complications in the remaining cohort. We will also determine whether any of the biomarkers studied could be responsible for the continued reduction in vascular events, retinopathy and nephropathy observed in the intensively treated arm of the cohort thus explaining the "metabolic imprint" recently postulated by the DCCT/EDIC group of investigators to explain the reduction of events induced by intensive glycemic control during the DCCT phase of the study, regardless of the similarity of glycemic control in the past decade.
