

BIOGRAPHICAL SKETCH

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NAME HUANG, Yan (MD, PhD)	POSITION TITLE		
eRA COMMONS USER NAME huangyan	Professor		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Shanghai Second Medical Univ., Shanghai, China	MD	1982	Medicine
Shanghai Sixth People's Hospital, Shanghai, China	Resident	1986	Internal Medicine
University of Cincinnati, Cincinnati, Ohio	MS	1989	Experimental Pathology
University of Cincinnati, Cincinnati, Ohio	PhD	1992	Experimental Pathology

A. Personal Statement

My research interest is the role of the innate immune responses in atherosclerosis and periodontal disease in diabetes with a focus on matrix metalloproteinases (MMPs) and proinflammatory cytokines. Recent studies have shown that the innate immune responses play an important role in diabetic complications. My research objective is to determine how the innate immune responses regulate MMP and cytokine expression and contribute to atherosclerosis and periodontal disease in diabetes and what are the underlying signaling mechanisms. I have an ongoing research project funded by VA Merit Review grant that studies the role of Toll-like receptors (TLRs), receptors for the innate immune responses, in atherosclerosis in diabetes. I have another ongoing research project funded by NIH RO1 grant that studies the effect of statin on diabetes-associated periodontal disease that is related to cardiovascular disease.

B. Positions and Honors

Positions and Employment:

1982-1986	Resident, Department of Medicine, Shanghai Sixth People's Hospital, Shanghai Second Medical University, Shanghai, China
1986-1992	Graduate Research Assistant with Dennis Sprecher (MD) and David Y. Hui (PhD) in the Atherosclerosis Laboratory, Department of Pathology, University of Cincinnati, Cincinnati, OH
1992-1993	Postdoctoral Research Fellow (supported by American Heart Association Postdoctoral Fellowship), Department of Pathology, University of Cincinnati, Cincinnati, OH
1993-1994	Postdoctoral Research Fellow, Laboratory of G.I. Hormones, Department of Surgery, University of Cincinnati, Cincinnati, OH
1995-2005	Assistant Professor, Division of Endocrinology, Diabetes, and Medical Genetics, Department of Medicine, Medical University of South Carolina (MUSC), Charleston, SC
2002-2005	VA Research & Development (R&D) Committee Member, Ralph H. Johnson VA Medical Center (VAMC), Charleston, SC
1998-Present	Faculty, College of Graduate Studies, MUSC, Charleston, SC
1999-Present	Research Health Scientist, VAMC, Charleston, SC
2005-Present	Faculty, College of Dental Medicine, MUSC, Charleston, SC
2005-Present	VA R&D, Subcommittee on Research Safety Member, VAMC, Charleston, SC
2006-Present	Associate Professor, Division of Endocrinology, Diabetes, and Medical Genetics, Department of Medicine, MUSC, Charleston, SC
2012-Present	Professor, Division of Endocrinology, Diabetes, and Medical Genetics, Department of Medicine, MUSC, Charleston, SC
2011-Present	VA Cardiovascular Disease Merit Grant Review Committee member, Department of VA

Honors:

1982	Honor graduate, Shanghai Second Medical University, Shanghai, China
1992	American Heart Association Postdoctoral Fellowship, awarded by the AHA, Ohio Affiliate
1999	Atorvastatin Research Award, awarded by Parke-Davis and Pfizer

C. Selected Peer-reviewed Publications (from 53 publications)

Most relevant to the current application

1. He L, Game BA, Nareika A, Garvey WT, Huang Y. Administration of Pioglitazone in Low-Density Lipoprotein Receptor-Deficient Mice Inhibits Lesion Progression and MMP Expression in Advanced Atherosclerotic Plaques. *Journal of Cardiovascular Pharmacology* 48:212-222, 2006.
2. Nareika A, Im Y, Game BA, Slate EH, Sanders JJ, London SD, Lopes-Virella MF, **Huang Y**, High glucose enhances lipopolysaccharide-stimulated CD14 expression in U937 mononuclear cells by increasing NFkB and AP-1 activities, *Journal of Endocrinology* 196:45-55, 2008.
3. Samuvel DJ, Sundararaj KP, Nareika A, Lopes-Virella MF, **Huang Y**. Lactate boosts TLR4 signaling and NFkB pathway-mediated gene transcription in macrophages via monocarboxylate transporters and MD-2 upregulation. *Journal of Immunology* 182:2476-2484, 2009.
4. Sundararaj KP, Samuvel DJ, Li Y, Sanders JJ, Lopes-Virella1 MF, **Huang Y**. IL-6 released from fibroblasts is essential for upregulation of MMP-1 expression by U937 macrophages in coculture – Cross-talking between fibroblasts and U937 macrophages exposed to high glucose. *Journal of Biological Chemistry*, 284:13714-13724, 2009.
5. Samuvel DJ, Sundararaj KP, Li Y, Lopes-Virella1 MF, **Huang Y**. Adipocyte-mononuclear cell interaction, Toll-like receptor 4 activation, and high glucose synergistically upregulate osteopontin expression via an interleukin 6-mediated mechanism. *Journal of Biological Chemistry* 285:3916-3927, 2010.
6. Li Y, Samuvel DJ, Sundararaj KP, Lopes-Virella MF, **Huang Y**. IL-6 and high glucose synergistically upregulate MMP-1 expression by U937 mononuclear phagocytes via ERK1/2 and JNK pathways and c-Jun. *Journal of Cellular Biochemistry* 110:248-259, 2010.
7. Lu Z, Li Y, Jin J, Zhang X, Lopes-Virella MF, **Huang Y**. TLR4 activation in microvascular endothelial cells triggers a robust inflammatory response and crosstalk with mononuclear cells via IL-6. *Arteriosclerosis, Thrombosis and Vascular Biology* 32:1696-1706, 2012.

Additional selected publications (in chronological order)

1. **Huang Y**, Ghosh M, Lopes-Virella MF. Transcriptional and post-transcriptional regulation of LDL receptor gene expression in PMA-treated THP-1 cells by LDL-containing immune complexes. *J. Lipid Research* 38:110-120, 1997.
2. **Huang Y**, Ayad J, Koskinen S, Takei A, Lopes-Virella MF. Oxidized LDL-containing immune complexes induce Fc gamma receptor I-mediated mitogen-activated protein kinase activation in THP-1 macrophages. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 19:1600-1607, 1999.
3. **Huang Y**, Mironova M, Lopes-Virella MF. Oxidized LDL stimulates matrix metalloproteinase-1 expression in human vascular endothelial cells. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 19:2640-2647, 1999.
4. **Huang Y**, Fleming AJ, Wu S, Virella G, Lopes-Virella MF. Fc gamma receptor cross-linking by immune complexes induces matrix metalloproteinase-1 in U937 cells via mitogen-activated protein kinase cascade. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 20:2533-2538, 2000.
5. Klein R, Ascencao JL, Mironova M, **Huang Y**, Lopes-Virella MF. Effect of inflammatory cytokines on the metabolism of low density lipoproteins by human vascular endothelial cells. *Metabolism* 50:99-106, 2001.
6. Takei A, **Huang Y**, Lopes-Virella MF. Intercellular adhesion molecule-1 (ICAM-1) expression induced by oxLDL on human umbilical vein endothelial cells (HUVEC) depends on the stage of LDL oxidation. *Atherosclerosis* 154:79-86, 2001.
7. **Huang Y**, Song L, Wu S, Fan F, Lopes-Virella MF. Oxidized LDL differentially regulates MMP-1 and TIMP-1 expression in human vascular endothelial cells. *Atherosclerosis* 156:119-125, 2001.
8. Song L, Lopes-Virella MF, and **Huang Y**. Quercetin inhibits oxidized LDL-stimulated matrix metalloproteinase-1 expression in endothelium by blocking extracellular signal regulated protein kinase. *Archives of Biochemistry and Biophysics* 391:72-78, 2001.
9. Anderson F, Xu M, Game BA, Atchley D, Lopes-Virella MF, **Huang Y**. IFN-g pre-treatment augments immune complex-induced matrix metalloproteinase-1 expression in U937 histiocytes. *Clinical Immunology* 102:200-207, 2002.
10. **Huang Y**, Fu Y, Bandyopadhyay S, Virella G, Lopes-Virella MF. LDL Immune Complexes Stimulate Low Density Lipoprotein Receptor Expression in U937 Histiocytes via Extracellular Signal-Regulated Kinase and AP-1. *Journal of Lipid Research* 44:1315-1321, 2003.

11. Game BA, Tang D, Minfu Xu, Lopes-Virella MF, **Huang Y**. Regulation of MMP-1 expression in vascular endothelial cells by insulin-sensitizing thiazolidinediones. *Atherosclerosis* 169:235-243, 2003.
12. Maldonado A, Game BA, Song L, **Huang Y**. Upregulation of matrix metalloproteinase-1 expression in U937 cells by LDL-containing immune complexes requires the AP-1 and Ets Motifs in the distal and the proximal promoter region. *Immunology* 109:572-579, 2003.
13. Williams TN, Zhang C, Game BA, He L, **Huang Y**. C-reactive protein stimulates MMP-1 expression in U937 histiocytes through FcgRII and ERK pathway. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 24:61-66, 2004.
14. Maldonado A, He L, Game BA, Nareika A, Sanders JJ, London SD, Lopes-Virella MF, Huang Y. Pre-Exposure to High Glucose Augments Lipopolysaccharide-Stimulated Matrix Metalloproteinase-1 Expression by Human U937 Histiocytes. *Journal of Periodontal Research* 39, 415-423, 2004.
15. Game BA, Maldonado A, Huang Y. Pioglitazone inhibits MMP-1 expression in vascular smooth muscle cells through a mitogen-activated protein kinase-independent mechanism. *Atherosclerosis* 178:249-256, 2005.
16. Kraml PJ, Klein RL, Huang Y, Nareika A, Lopes-Virella MF. Iron Loading Increases Cholesterol Accumulation and Macrophage Scavenger Receptor-I Expression in THP-I Mononuclear Phagocytes. *Metabolism* 54:453-459, 2005.
17. Song W, Barth JL, Lu K, Yu Y, Huang Y, Gittinger CK, Argraves WS, Lyons TJ. Effects of oxidized and glycated LDL on gene expression in human retinal capillary pericytes, *Investigative Ophthalmology & Visual Science*, 46:2974-2982, 2005.
18. Song W, Barth JL, Lu K, Yu Y, Huang Y, Gittinger CK, Argraves WS, Lyons TJ. Effects of modified low-density lipoproteins on human retinal pericyte survival. *Ann NY Acad Sci.* 1043:390-395, 2005.
19. Nareika A, He L, Game BA, Slate EH, Sanders JJ, London SD, Lopes-Virella MF, **Huang Y**. Sodium lactate increases LPS-stimulated MMP and cytokine expression in U937 histiocytes by enhancing AP-1 and NFkB transcriptional activities. *American Journal of Physiology (Endocrinology and Metabolism)* 289:E534-E542, 2005.
21. Nareika A, Maldonado A, He L, Game BA, Slate EH, Sanders JJ, London SD, Lopes-Virella MF, **Huang Y**. High Glucose-Boosted Inflammatory Responses to Lipopolysaccharide Are Suppressed by Statin. *Journal of Periodontal Research* 42:31-38, 2006.
22. Game BA, He L, Jarido V, Nareika A, Jaffa AA, Lopes-Virella MF, **Huang Y**. Pioglitazone inhibits connective tissue growth factor expression in advanced atherosclerotic plaques in low-density lipoprotein receptor-deficient mice. *Atherosclerosis* 192:85-91, 2007.
23. Barth JL, Yu Y, Song W, Lu K, Dashti A, **Huang Y**, Argraves WS, Lyons TJ. Oxidised, glycated LDL selectively influences tissue inhibitor of metalloproteinase-3 gene expression and protein production in human retinal capillary pericytes. *Diabetologia* 50:2200-2208, 2007.
24. Cole CM, Sundararaj KP, Leite RS, Nareika A, Slate EH, Sanders JJ, Lopes-Virella MF, **Huang Y**. A trend of increase in periodontal IL-6 expression across patients with neither diabetes nor periodontal disease, patients with periodontal disease alone, and patients with both diseases. *Journal of Periodontal Research* 43:717-722, 2008.
25. Sundararaj KP, Samuvel DJ, Li Y, Nareika A, Slate EH, Sanders JJ, Lopes-Virella MF, **Huang Y**. Simvastatin suppresses LPS-induced MMP-1 expression in U937 mononuclear cells by inhibiting protein isoprenylation-mediated ERK activation, *Journal of Leukocyte Biology*,84:1120-1129, 2008.
26. Nareika A, Sundararaj KP, Im Y, Game BA, Lopes-Virella MF, **Huang Y**. High glucose and interferon gamma synergistically stimulate MMP-1 expression in U937 macrophages by increasing transcription factor STAT1 activity. *Atherosclerosis*, 202:363-371, 2009.
27. Ross JH, Hardy DC, Schuyler CA, Slate EH, Mize TW, **Huang Y**. Periodontal IL-6 protein expression is increased across patients with neither periodontal disease nor diabetes, patients with periodontal disease alone, and patients with both diseases. *Journal of Periodontal Research* 45:688-694, 2010.
28. Ta NN, Li Y, Schuyler CA, Lopes-Virella MF, **Huang Y**. DPP-4 (CD26) inhibitor alogliptin inhibits TLR4-mediated ERK activation and ERK-dependent MMP-1 expression by U937 histiocytes. *Atherosclerosis* 213:429-435, 2010.
29. Abdelsamie SA, Li Y, **Huang Y**, Lee M, Klein RL, Virella G and Lopes-Virella MF. Oxidized LDL Immune Complexes Stimulate Collagen IV Production in Mesangial Cells via Fc Gamma Receptors I and III. *Clinical Immunology* 139:258-266, 2011.

30. Schuyler CA, Ta NN, Li Y, Lopes-Vireall MF, **Huang Y**. Insulin Treatment Attenuates Diabetes-Increased Atherosclerotic Intimal Lesions and Matrix Metalloproteinase-9 Expression in Apolipoprotein E-Deficient Mice, *Journal of Endocrinology* 210:37-46, 2011.
31. Ta NN, Schuyler CA, Li Y, Lopes-Virella MF, **Huang Y**. DPP-4 (CD26) inhibitor alogliptin inhibits atherosclerosis in diabetic apolipoprotein E-deficient mice, *Journal of Cardiovascular Pharmacology* 58:157-166, 2011.
32. Samuvel DJ, Junfei Jin, Sundararaj KP, Li Y, Xiaoming Zhang Lopes-Virella MF, **Huang Y**. TLR4 Activation and IL-6-Mediated Crosstalk between Adipocytes and Mononuclear Cells Synergistically Stimulate MMP-1 Expression. *Endocrinology* 152:4662-4671, 2011.
33. Jin J, Samuvel DJ, Zhang X, Li Y, Lu Z, Lopes-Virella MF, **Huang Y**. Coactivation of TLR4 and TLR2/6 Coordinates an Augmentation on IL-6 Gene Transcription via p38 MAPK Pathway in U937 Mononuclear Cells. *Molecular Immunology* 49:423-432, 2011.
34. Hardy DC, Ross JH, Schuyler CA, Leite RS, Slate EH, **Huang Y**. MMP-8 expression in periodontal tissues surgically removed from diabetic and nondiabetic patients with periodontal disease, *Journal of Clinical Periodontology*, 39:249-255, 2012.
35. Jin J, Sundararaj KP, Samuvel DJ, Zhang X, Li Y, Lu Z, Lopes-Virella MF, **Huang Y**. Different signaling mechanisms regulating IL-6 expression by LPS between gingival fibroblasts and mononuclear cells: Seeking the common target. *Clinical Immunology*, 143:188-199, 2012.

D. Research Support

Ongoing Research Support:

2R01 DE016353-06A1 Huang (PI)

11/01/2004-04/30/2015

NIH/NIDCR

The Effect of Statin on Diabetes-Associated Periodontal Disease

The goal of this research project is to provide novel information for better understanding of the effects of statin on periodontal disease in both nondiabetic and diabetic patients, which is important for potential use of statins in treatment of periodontal disease as proposed by AAP.

1I01 BX000854-01A1 Huang (PI)

10/01/2010-09/30/2014

Department of Veterans Affairs, ORD

BLRD Merit Award - Biomedical Laboratory R&D Program

Toll-Like Receptors and Atherosclerosis in Diabetes

This study will establish whether there is a rationale for targeting TLR4 in prevention of cardiovascular event in patients with diabetes or metabolic syndrome. This studies are expected to provide important information for developing a new therapeutic strategy to prevent fatal cardiovascular events in our Veterans with diabetes.

Role: PI

Completed Research Support (last 3yrs):

R01 DE016353 Huang (PI)

11/01/2004-04/30/2010

NIH/NIDCR

Diabetes and Periodontal Gene Expression

The goal of this research project is to determine the relationship between diabetes and periodontal expression of matrix metalloproteinase and inflammatory cytokines and the underlying mechanisms.

N/A Huang (PI)

04/01/2007-03/31/2010

Department of Veterans Affairs, ORD

VA Merit Review Grant

Diabetes and the Stability of Atherosclerotic Plaques

The goal of this study is to determine the impact of diabetes-associated factors such as hyperglycemia on the stability of atherosclerotic plaques in diabetic animal model.

08-003ALO Huang (PI)

02/01/2009-01/31/2011

Takeda Pharmaceutical North America, Inc.

The Effect of Alogliptin on Vascular Inflammation and Atherosclerosis

The goal of this study is to determine the effects of alogliptin on the progression of atherosclerotic plaques and plaque pro-inflammatory gene expression.

