Curriculum Vitae
Chiang-Ching Spencer Huang, Ph.D.

PERSONAL INFORMATION

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EDUCATION

University of Michigan, Ann Arbor, MI August 2003
Ph.D. in Biostatistics
University of Iowa, Iowa City, IA June 1998
Master of Science in Statistics
National Chiao-Tung University, Hsinchu, Taiwan June 1987
Bachelor of Science in Applied Mathematics

POSITION and EXPERIENCE

Associate Professor
Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University — September 2012 – Present

Director, Bioinformatics Research Collaboratory September 2012 –Present
Feinberg School of Medicine, Northwestern University

Assistant Professor September 2003–August 2012
Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University

Director, Public Health Informatics July 2007– October 2010
Northwestern University Biomedical Informatics Center

PROFESSIONAL and SCIENTIFIC SERVICE

Genetics/Genomics Committee September 2007–Present
Multi-Ethnic Study of Atherosclerosis (MESA) (NIH/NHLBI)

Genomics Committee October 2007–October 2009
Hispanic Community Health Study (NIH/NHLBI)

Genetics Committee October 2008–Present
Longitudinal Studies of Coronary Artery Risk Development in Young Adults (CARDIA) (NIH/NHLBI)

Ad hoc Reviewer, National Health Research Institutes (NHRI) Extramural Grant Scientific Review 2013

Reviewer, NIH/NIGMS Special Emphasis Panel August, 2009
Grand Opportunities (GO) grant applications in response to the NIGMS topic:
"Leukocyte Gene Expression in Healthy Humans"

Scientific program committee June 2010
International Chinese Statistical Association

Scientific Conference Session Organizer
"Statistical Issues in Analyzing Emerging Genomic Data"
The 19th International Chinese Statistical Association Applied Statistics Symposium June 2010
"Coronary Artery Disease Risk Factors"
The 3rd Annual International Congress of Cardiology July 2011

Abstract Grader
American Heart Association Scientific Sessions, 2008, 2009, 2010, 2011, 2012, 2013

Journal Peer-Reviewer
Journal of the American Medical Association, Analytic Chemistry, Archives of Internal Medicine, Arthritis & Rheumatism, Bioinformatics, BMC Medical Genomics, Cancer Informatics, Circulation, Circulation Research, Genomics, Trends in Biotechnology, PLoS ONE, Journal of Proteome Research

AWARDS, HONORS, DISTINCTIONS

Best Poster in Population Science November 2008, Chicago
2008 American Heart Association Scientific Poster Competition: "A Genomic Signature of Atherosclerosis among Individuals with Low Framingham Risk Score: The Multi-Ethnic Study of Atherosclerosis (MESA)"

TEACHING

STAT 465: Statistical Methods for Computational Biology and Bioinformatics (Guest lecturer)
Department of Statistics, Northwestern University Fall term 2003–2005

EPI BIO 499: Statistical Consultation August–December, 2007
MS in Epidemiology and Biostatistics (MSEB) Program
Department of Preventive Medicine, Northwestern University

Summer Course: R in Bioinformatics July, 2008
National Taiwan University

MSCI 490: Independent Study in Genetic Epidemiology April–June 2009
MS in Clinical Investigation (MSCI) Program
Northwestern University Clinical and Translational Sciences (NUCATS) Institute

EPI BIO 502: Advanced Biostatistics September–December 2009
MS in Epidemiology and Biostatistics (MSEB) Program
Department of Preventive Medicine, Northwestern University

EPI BIO 428: Bioinformatics and Data Mining April–June 2011
MS in Epidemiology and Biostatistics (MSEB) Program
Department of Preventive Medicine, Northwestern University

MSCI 428: Introduction to Bioinformatics January–April 2013
MS in Clinical Investigation (MSCI) Program
Northwestern University Clinical and Translational Sciences (NUCATS) Institute

Fellow, Northwestern Searle Center for Teaching Excellence August 2009–June 2010

Mentoring Experience:
Simone Treiger Sredni, MD, PhD Mentor since June 2007
Assistant Professor
Department of Pediatrics, Feinberg School of Medicine, Northwestern University
Center for Excellence in Clinical Immunology
Neurosurgery Research Program, Children's Memorial Research Center

Monique Hinchcliff, MD Mentor since July 2008
Assistant Professor of Medicine
Division of Rheumatology, Department of Medicine
Feinberg School of Medicine, Northwestern University

Rosemary Braun, PhD
Assistant Professor Mentor since January 2012
Department of Preventive Medicine
Feinberg School of Medicine, Northwestern University

Yinan Zhang, MS Academic Advisor since August 2012
PhD student in Walter S. and Lucienne Driskill
Graduate Training Program in Life Sciences
Feinberg School of Medicine, Northwestern University

RESEARCH GRANTS/CONTRACTS

Active Research Support:

5R01 NR012692 (Pachman) 09/29/10 – 07/31/14
NIH/NINR
Disease Chronicity in Juvenile Dermatomyositis (JDM): Epigenetic Clues
The purpose of this study is to identify epigenetic mechanisms - differences in global methylation and miRNA expression - critical in dissecting the impact of chronic inflammation and gender on JDM microvasculopathy. In this study, the quality of life of the children with JDM will be determined and correlated with their epigenetic status - inherited changes in phenotype determined by genes and the environment - by testing diagnostic muscle biopsies from untreated children with JDM with long compared with short disease duration and age-, gender-matched healthy controls.
Role: Co-Investigator/Subcontract PI

P60 AR048098-09 (Pope/Chang) 08/01/07 – 07/31/13

NIH/NIAMS
Multidisciplinary Clinical Research Center in Rheumatology
The goals of the Northwestern University Multidisciplinary Clinical Research Center in Rheumatology are: 1) to conduct cutting-edge, nationally recognized and funded research aimed at the prevention or control of arthritis and musculoskeletal diseases; and 2) to provide the academic environment that supports and enhances the interdisciplinary research of the MCRC faculty.
Role: Co-Investigator

N01-HC-95164 (Liu) 01/15/10 – 08/14/15
NIH/NHLBI
Multi-Ethnic Study of Atherosclerosis (MESA)
The primary objective of this project is to conduct a longitudinal study in a representative population-based sample of 6,800 White, Black, Hispanic, and Asian men and women ages 45-84 at baseline to: a) evaluate various measures of subclinical cardiovascular disease (CVD); b) examine factors associated with progression of subclinical CVD to overt disease; and c) develop population-based methods for identifying high-risk asymptomatic persons for prevention and intervention.
Role: Co-Investigator

N01-HC-48049 (Liu) 12/20/07 – 07/31/13
NIH/NHLBI
Longitudinal Studies of Coronary Artery Risk Development in Young Adults (CARDIA)
CARDIA is a 4-center national collaborative longitudinal investigation of physiological, psychological, and other factors which may influence the evolution of coronary heart disease risk factors in young black and white men and women initially ages 18-30 in 1985-1986.
Role: Co-Investigator

(Hinchcliff) 07/01/11 – 06/30/14
Scleroderma Foundation
Measuring Gene Expression in the Skin: Novel Biomarkers for Scleroderma
The experiments in this proposal will test whether DNA microarray analyses of skin can predict response to mycophenolate mofetil (MMF). The goal is to identify a subset of genes whose expression changes during MMF treatment and uncover the dysregulated molecular pathways that may be involved in scleroderma (SSc).
Role: Co-Investigator

5 P30 CA060553-17 (Rosen) 09/14/07 - 07/31/13
NIH/NCI
The Robert H. Lurie Comprehensive Cancer Center
The goals of this Cancer Center Support Grant are to conduct and support cancer research and to integrate cancer-related research throughout the university; to coordinate and integrate cancer-related activities of the University including community outreach initiatives; to develop and conduct cancer education programs; to promote and participate in state-of-the-are care of cancer patients at the affiliated hospitals of the McGaw Medical Center of Northwestern University and; to develop and implement the initiatives in cancer prevention and control research. These goals are accomplished through the activities of the 10 establish programs and 13 shared resources.
Role: Biostatistician

5 P30 CA060553-17 (Rosen) 09/01/12 – 07/31/13

NIH/NCI
The Robert H. Lurie Comprehensive Cancer Center
The mission of this core facility will be to provide bioinformatics capabilities to best serve the needs for the basic and translational research community in the cancer center.
Role: Co-Investigator/Director of Bioinformatics Core

Completed Research Support:

U10 CA98543 (Perlman/Huang) 09/01/09 – 10/31/12
NIH/NCI
The Therapeutically Applicable Research to Generate Effective Treatments (TARGET): Analysis of High Risk Wilms' Tumor
This project was to interrogate the genomic, transcriptomic, epigenomic, and mutational characteristics of high risk Wilms' tumors treated on NWTSG/COG protocols using microarray and next generation DNA sequencing technology. The goal is to 1) identify genetic mutations involved in the pathogenesis of Wilms' tumor, and in the development of relapse and anaplasia; 2) assess genomic gains and losses in relapse favorable histology Wilms tumor (RFHWT) and unfavorable histology Wilms' tumor (UFWT); 3) define transcription patterns within RFHWT and UFWT; 4) define activated pathways in RFHWT, UFWT, and favorable histology Wilms' tumor (FHWT).
Role: Subcontract Principal Investigator

RC1 ES018461-02 (Hou) 09/27/09 – 07/31/11
NIH/NIEHS
DNA Methylation Alterations in Response to Pesticide Exposures
This project was to study whether Organophosphate Pesticides (OP) exposure alters gene promoter DNA methylation patterns in human subjects, and in OP-treated cell lines.
Role: Co-Investigator

R01 HL084228 (Stamler) 02/01/07 – 01/31/11
NIH/NHLBI
Metabolomics-Measured Urinary Metabolites, Diet & BP, 17 Population Samples: INTERMAP
The goal of this project is to investigate how nutrient intake influences metabolomic patterns and to identify urinary metabolite biomarkers in relation with blood pressure using H^1 NMR metabolomic profiles of 4,670 individuals in the INTERMAP cohort.
Role: Co-Investigator

U01 CA114757 (Perlman/Huang) 06/01/05 – 05/30/10
NIH/NCI
Strategic Partnering to Evaluate Cancer Signatures (SPECS): Diagnostic and Prognostic Sarcoma Signatures
This is a multi-institutional collaborative project. The goal of this project was to confirm and refine previously identified molecular signatures of pediatric sarcomas for treatment response or diagnosis using modern high throughput genomics technologies.
Role: Subcontract Principal Investigator

R01 HL086678 (Huang) 03/15/07 – 02/28/10
NIH/NHLBI
Atherosclerosis Risk Refinement: A Multi-Marker Approach Using Microarrays

The goal of this project was to use gene expression profiles of peripheral blood to identify atherosclerosis-related pathways and gene signatures that can improve risk stratification among individuals with low CVD 10-year predicted risk.
Role: Principal Investigator

U01 CA088131 (Perlman/Huang) 12/01/04-11/30/06
NIH/NCI
Categorization of Wilms' Tumor by Genetic Expression
This project was to 1) identify new molecular categories of Wilms' tumor (WT) based on the gene expression profiles of samples from patients with this disease; 2) Develop a classification system (classifier) that will predict a defined number of clinically relevant categories based on expression of an established set of genes.
Role: Subcontract Principal Investigator

SCHOLARLY BIBLIOGRAPHY

Peer-Reviewed Research Papers (* corresponding author, †key bioinformatician/biostatistician)

1. Chen G, Gharib TG**, Huang CC**†, Taylor JM, Misek DE, Kardia SL, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, and Beer DG. Discordant Protein and mRNA Expression in Lung Adenocarcinomas**.** *Mol Cell Proteomic.* 2002, 1:314-22.
2. Beer DG, Kardia SL, **Huang CC**†, Levin AM, Misek DE, Lin L, Chen G, Gharib TG, Thomas DG, Giordano TJ, Lizyness ML, Kuick R, Hayasaka S, Taylor JM, Iannettoni MD, Orringer MB, Hanash S. Gene Expression Profiles Predict Survival in Lung Adenocarcinomas. *Nat Med.* 2002, 8, 816-24.
3. Gharib TG, Chen G, Wang H, **Huang CC**, Prescott MS, Shedden KA, Misek DE, Thomas DG, Giordano TJ, Taylor JM, Kardia S, Yee J, Orringer MB, Hanash S, Beer DG. Proteomic Analysis of Cytokeratin Isoforms Uncovers Association with Survival in Lung Adenocarcinoma. *Neoplasia.* 2002, 4(5), 440-8.
4. Moran CJ, Arenberg DA, **Huang CC**†**,** Giordano TG, Thomas DG, Misek DE, Chen G, Iannettoni, MD, Orringer MB, Hanash S, Beer DG. RANTES Expression Is a Predictor of Survival in Stage I Lung Adenocarcinoma. *Clin Cancer Res*. 2002, 8:3803-12.
5. Chen G, Gharib TJ, **Huang CC**†, Thomas DG, Shedden KA, Taylor JM, Kardia SL, Misek DE, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, and Beer DG. Proteomic Analysis of Lung Adenocarcinoma: Identification of a Highly Expressed Set of Proteins in Tumors. *Clin Cancer Res.* 2002, 8: 2298-305.
6. Chen G, Wang H, Gharib TG, **Huang CC**, Thomas DG, Shedden KA, Kuick R, Taylor JM, Kardia SL, Misek DE, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, and Beer DG. Overexpression of Oncoprotein 18 Correlates with Poor Differentiation in Lung Adenocarcinomas. *Mol Cell Proteomics*. 2003, 2(2):107-16.
7. Chen G, Gharib TG, Thomas DG, **Huang CC**, Misek DE, Kuick RD, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, and Beer DG. Proteomic Analysis of EIF-5A in Lung Adenocarcinomas. *Proteomics*. 2003, 3(4):496-504.
8. Schwartz DR, Wu R, Kardia SL, Levin AM, **Huang CC**, Shedden KA, Kuick R, Misek DE, Hanash SM, Taylor JM, Reed H, Hendrix N, Zhai Y, Fearon ER, Cho KR. Novel Candidate Targets of ß-catenin/TCF Signaling Identified by Gene Expression Profiling of Ovarian Endometrioid Adenocarcinomas. *Cancer Res.* 2003, 63(11):2913-22.
9. Chen G, Gharib TG, Wang H, **Huang CC**†, Kuick R, Thomas DG, Shedden KA, Misek DE, Taylor JM, Giordano TJ, Kardia SL, Iannettoni MD, Yee J, Hogg PJ, Orringer MB, Hanash SM, and Beer DG. Protein Profiles Associated with Survival in Lung Adenocarcinoma. *PNAS.* 2003, 100(23):13537-42.
10. Gharib TG, Chen G, **Huang CC**†, Misek DE, Iannettoni MD, Hanash SM, Orringer MB, Beer DG. Genomic and Protemic Analyses of Vascular Endothelial Growth Factor and Insulin-Like Growth

Factor-Binding Protein 3 in Lung Adenocarcinomas. *Clin Lung Cancer*. 2004, 5(5):307-12.
11. Pasche B, Knobloch TJ, Bian Y, Liu J, Phukan S, Rosman D, Kaklamani V, Baddi L, Siddiqui FS, Frankel W, Prior TW, Schuller DE, Agrawal A, Lang J, Dolan ME, Vokes EE, Lane WS, **Huang CC,** Caldes T, Cristofano AD, Hampel H, Nilsson I, Gunnar von Heijne, Fodde R, Murty VVVS, Albert de la Chapelle, Weghorst CM. Somatic Acquisition and Signaling of *TGFBR1**6A in Cancer. *JAMA.* 2005, 294:1625-33.
12. Cutcliffe C, Kersey D, **Huang CC**†, Zeng Y, Walterhouse D, Perlman EJ for the Renal Tumor Committee of the Children's Oncology Group. Clear Cell Sarcoma of the Kidney: Up-regulation of Neural Markers with Activation of the Sonic Hedgehog and Akt Pathways. *Clin Cancer Res.* 2005, 11: 7986-94.
13. **Huang CC**, Cutcliffe C, Coffin C, Sorensen P, Beckwith JB, Perlman EJ for the Renal Tumor Committee of the Children's Oncology Group. Classification of Malignant Pediatric Renal Tumors by Gene expression. *Pediatr Blood Cancer.* 2006, 46:728-38.
14. Amin SA, **Huang CC**†, Reierstad S, Lin Z, Arbieva Z, Wiley E, Saborian H, Haynes B, Cotterill H, Dowsett M, Bulun SE. Paracrine-Stimulated Gene Expression Profile Favors Estradiol Production in Breast Tumors. *Mol Cell Endocrinol.* 2006, 253(1-2):44-55.
15. **Huang CC***, Taylor JM, Beer DG, Kardia SL. Hidden Markov Model for Defining Genomic Changes in Lung Cancer Using Gene Expression Data. *OMICS. 2006*, 10(3): 276-88.
16. Lin Z, Reierstad S, **Huang, CC**†, Bulun SE. Novel Estrogen Receptor-alpha Binding Sites and Estradiol Target Genes Identified by Chromatin Immunoprecipitation Cloning in Breast Cancer. *Cancer Res.* 2007, 67(10): 5017-24.
17. Wang J, Jarrett J, **Huang CC**†, Satcher RL Jr, Levenson AS. Identification of Estrogen-responsive Genes Involved in Breast Cancer Metastases to the Bone. *Clin Exp Metastasis*. 2007, 24(6): 411-22.
18. Xue Q, Lin Z, Cheng YH, **Huang CC**, Yin P, Reierstad S, Marsh E, Milad MP, Confino E, Innes J, Bulun S. Promoter Methylation Regulates Estrogen Receptor 2 Expression in Endometrium. *Bio. Reprod.* 2007, 77(4):681-7.
19. Liu H, Shi B, **Huang CC**†, Eksarko P, Pope RM. Transcriptional Diversity during Monocyte to Macrophage Differentiation. *Immunol Lett*. 2008, 117(1):70-80.
20. Rosman D, Phukan S, **Huang CC**†, Pasche B. TGFBR1*6A Enhances the Migration and Invasion of MCF-7 Breast Cancer Cells through RhoA Activation. *Cancer Res.* 2008, 68(5), 1319-28.
21. Zeng Q, Phukan S, Xu Y, Sadim M, Rosman DS, Liao J, Zhang M, Yang G-Y, **Huang CC**, Valle L, Cristofano AD, Chapelle A, Pasche B. *Tgfbr1* Haploinsufficiency Enhances *Apc*-mediated Colon Cancer Development. *Cancer Res*. 2009, 69(2):678-86.
22. Brown IJ, Elliott P, Robertson CE, Chan Q, Daviglus ML, Dyer AR, **Huang CC**, Rodriguez BL, Sakata K, Ueshima H, Van Horn L, Zhao L, Stamler J, for the INTERMAP Research Group. Dietary Starch Intake of Individuals and Their Blood Pressure: the International Study of Macronutrients and Micronutrients and Blood Pressure. *J Hypertens.* 2009, 27:231-6.
23. **Huang CC**, Gadd S, Breslow N, Cutcliffe C, Sredni ST, Helenowski IB, Dome JS, Grundy PE, Green DM, Fritsch MK, Perlman EJ. Predicting Relapse in Favorable Histology Wilms Tumor Using Gene Expression Analysis: A Report from the Renal Tumor Committee of the Children's Oncology Group. *Clin Cancer Res*. 2009, 15(5):1770-8.
24. **Huang CC**, Fornage M, Lloyd-Jones DM, Wei GS, Boerwinkle E, Liu K. Longitudinal Association of PCSK9 Sequence Variations with LDL-Cholesterol Levels: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Circ Cardiovasc Genet*. 2009, 2(4): 354-361.
25. Sredni ST, Gadd S, **Huang CC**†, Breslow N, Grundy P, Green DM, Dome JS, Shamburge RC, Beckwith JB, and Perlman EJ. Subset of Very Low Risk Wilms Tumors Show Distinct Gene Expression, Histologic, and Clinical Features. *Clin Cancer Res*. 2009, 15(22): 6800-9.
26. Sredni ST, Bonaldo MD, Costa FF, **Huang CC**, Hamm CA, Rajaram V, Tomita T, Goldman S, Bischof JM, Soares MB. Brief communication - Upregulation of mir-221 and mir-222 in Atipical Teratoid/ Rhabdoid Tumors: Potental Therapeutic Targets. *Childs Nerv Syst.* 2010, 26(3):279-83.

27. Gadd S, Sredni ST, **Huang CC**†, Perlman EJ. Rhabdoid Tumor: Gene Expression Clues to Pathogenesis and Potential Therapeutic Targets. *Lab Invest.* 2010, 90(5):724-38.
28. Desai J, Flatow JM, Song J, Zhu LJ, Du P, **Huang CC**, Lu H, Lin SM, Kibbe WA. Visual Presentation as a Welcome Alternative to Textual Presentation of Gene Annotation Information. *Adv Exp Med Biol.* 2010, 680:709-15.
29. Chadeau-Hyam M, Ebbels TM, Brown IJ, Chan Q, Stamler J, **Huang CC**, Daviglus ML, Ueshima H, Zhao L, Holmes E, Nicholson JK, Elliott P, De Iorio M. Metabolic Profiling and the Metabolome-wide Association Study: Significance Level for Biomarker Identification. *J Proteome Res.* 2010, 9(9):4620-7.
30. Du P, Zhang X, **Huang CC**, Jafari N, Kibbe WA, Hou L, Lin SM. Comparison of Beta-value and M-value Methods for Quantifying Methylation Levels by Microarray Analysis. *BMC Bioinformatics*. 2010, 11:587.
31. Katz BZ, Salimi B, Gadd SL, **Huang CC**†, Kabat WJ, Kersey D, McCabe C, Heald-Sargent T, Katz ED, Yogev R. Differential Gene Expression of Soluble CD8+ T-cell Mediated Suppression of HIV Replication in Three Older Children. *J Med Virol.* 2011, 83(1):24-32.
32. Brown IJ, Stamler J, Van Horn L, Robertson CE, Chan Q, Dyer AR, **Huang CC**, Rodriguez BL, Zhao L, Daviglus ML, Ueshima H, Elliott P; for the International Study of Macro/Micronutrients and Blood Pressure Research Group. Sugar-Sweetened Beverage, Sugar Intake of Individuals, and Their Blood Pressure: International Study of Macro/Micronutrients and Blood Pressure. *Hypertension*. 2011, 57(4):695-701.
33. Sredni ST, **Huang CC**†, Bonaldo MD, Tomita T. MicroRNA Expression Profiling for Molecular Classification of Pediatric Brain Tumors. *Pediatr Blood Cancer.* 2011, 57(1): 183-4.
34. **Huang CC***, Liu K, Pope RM, Du P, Lin S, Rajamannan NM, Huang Q, Jafari N, Burke GL, Post W, Watson KE, Johnson C, Daviglus, M, Lloyd-Jones DM. Activated Toll-like Receptor Signaling in Atherosclerosis Among Women with Lower Framingham Risk Score: the Multi-Ethnic Study of Atherosclerosis. *PLoS ONE*. 2011, 6(6):e21067.
35. **Huang CC***, Lloyd-Jones DM, Guo X, Rajamannan NM, Lin S, Du P, Huang Q, Hou L, Liu K. Gene Expression Variation Between African Americans and Whites Is Associated with Coronary Artery Calcification: the Multi-Ethnic Study of Atherosclerosis. *Physiol Genomics.* 2011, 43(13): 836-43.
36. Sredni ST, Gadd S, Jafari N, **Huang CC*.** A Parallel Comparison of mRNA and microRNA Profiling of Peripheral Blood in Young Adult Women. *Frontiers in Genetics*. 2:49. doi: 10.3389/fgene.2011. 00049, July 2011.
37. Kuo CH, Wang KC, Tian TF, Tsai MH, Chiung YM, Hsiech CM, Tsai SJ, Wang SY, Tsai DM, **Huang CC**, Tseng YJ. Metabolomic Characterization of Laborers Exposed to Welding Fumes. *Chem Res Toxicol.* 2012, 25(3): 276-86.
38. Gadd S, Beezhold P, Jennings L, George D, Leuer K, **Huang CC**, Huff V, Tognon C, Sorensen PH, Triche T, Coffin CM, Perlman EJ. Mediators of Receptor Tyrosine Kinase activation in infantile fibrosarcoma: a Children's Oncology Group study. *J Pathol.* 2012, 228(1): 119-30. Feb 28.
39. Shi B, Huang Q, Tak PP, Vervoordeldonk MJ, **Huang CC**, Dorfleutner A, Stehlik C, Pope RM. SNAPIN: an endogenous Toll-like receptor ligand in rheumatoid arthritis. *Ann Rheum Dis.* 2012, 71(8):1411-7.
40. Hinchcliff M, **Huang CC**†, Ishida W, Fang F, Lee J, Jafari N, Wilkes M, Bhattacharyya S, Leof E, Varga J. Imatinib mesylate causes genome-wide transcriptional changes in systemic sclerosis fibroblasts in vitro. *Clin Exp Rheumatol*. 2012, 30(2 Suppl 71):S86-96.
41. Gadd S, Huff V, **Huang CC**†, Ruteshouser EC, Dome JS, Grundy PE, Breslow N, Jennings L, Green DM, Beckwith JB, Perlman EJ. Clinically Relevant Subsets Identified by Gene Expression Patterns Support a Revised Ontogenic Model of Wilms Tumor: A Children's Oncology Group Study. *Neoplasia*. 2012, 14(8):742-56.
42. Hinchcliff M, **Huang CC**†, Wood TA, Matthew Mahoney J, Martyanov V, Bhattacharyya S, Tamaki Z,

Lee J, Carns M, Podlusky S, Sirajuddin A, Shah SJ, Chang RW, Lafyatis R, Varga J, Whitfield ML. Molecular Signatures in Skin Associated with Clinical Improvement during Mycophenolate Treatment in Systemic Sclerosis. *J Invest Dermatol*. 2013 Mar 14. doi: 10.1038/jid.2013.130. [Epub ahead of print]

43. Quiñones R, Morgan GA, Amoruso M, Field R, **Huang CC**[†], Pachman LM. Four-year-olds, healthy or recovering from Juvenile Dermatomyositis, do not achieve a full score on the Childhood Myositis Assessment Scale (CMAS). *Arthritis Care Res* (Hoboken). 2013 May 10:NA. doi: 10.1002/acr.22041. [Epub ahead of print]
44. **Huang CC**, McDermott MM, Liu K, Kuo CH, Wang SY, Tao H, Tseng YJ. Plasma metabolomic profiles predict near-term death among individuals with lower extremity peripheral arterial disease. *J Vasc Surg*. 2013 May 17. doi:pii: S0741-5214(13)00799-4. 10.1016/j.jvs.2013.04.022. [Epub ahead of print]

Editorials

Huang CC, Bredel M. Use of Gene Signatures to Improve Risk Estimation in Human Cancer. *JAMA.* 2008, 299(13), 1605-7.

Book Chapters

Jennings L and **Huang CC**. "Expression Profiling in Pediatric Acute Leukemias". *Diagnostic Pediatric Hematopathology*, 2011, Cambridge.

PRESENTATIONS

Invited Presentations

1. "Omics: the Future for Personalized Medicine". *Utah ASA Chapter, Provo, UT, Feb. 2004.*
2. "Markov Model for Defining Genomic Changes in Cancer Using Microarray Data". *ENAR Statistical Meetings, Pittsburg, PA, March 2004.*
3. "Prognosis of Non-small Cell Lung Cancer Using Gene Expression Profiles". *Northwestern Bioinformatics Mini Symposium, Evanston, IL, July 2004.*
4. "Nutri-Metabolomics and Epidemiology – Personalized Nutrition". *Northwestern University, Chicago, IL, June 2006.*
5. "Robustness of cancer prognostic markers using gene expression microarrays". *Joint Statistical Meetings 2007, Salt Lake City, UT, July 2007.*
6. "Functional Genomics and Personalized Medicine". *Fuzhou Medical University, Fuzhou, China, Sept 2007.*
7. "Identification of Robust Genomic Signatures via Multiple Cross Validation". *Emerging Information and Technology Bioinformatics and Biomedical Research Symposium 2008, Princeton, NJ, June 2008.*
8. "Association of Aspartame and Aspartic Acid Intake with Body Mass Index: the INTREMAP Study". *Joint Conference - 49th Cardiovascular Disease Epidemiology and Prevention -and- Nutrition, Physical Activity and metabolism, Tampa, FL, March 2009.*
9. "Longitudinal Association of PCSK9 Sequence Variations with LDL-Cholesterol Levels: The Coronary Artery Risk Development in Young Adults (CARDIA) Study". *PCSK9 Conference, Nantes, France, March 2010.*
10. "Methylation Detection Call for Whole Genome Methylation Data". *ICSA 2010 Applied Statistics Symposium. Indianapolis, IN, June 2010.*
11. "Gene Expression Variation Between African Americans and Whites Is Associated with Coronary Artery Calcification: the Multi-Ethnic Study of Atherosclerosis." *Joint Conference – 51st*

Cardiovascular Disease Epidemiology and Prevention -and- Nutrition, Physical Activity and Metabolism, Atlanta, GA, March 2011.

12. "Application of Bioinformatics to Human Diseases – Roadmap to Discovery." *Beigene Inc., Philadelphia, PA, September 2011.*
13. "Activated TLR Signaling in Atherosclerosis Among Women with Lower Framingham Risk Score." *BIT's 3rd Annual International Congress of Cardiology, Beijing, China, December 2011.*
14. *"*Meta analysis of transcriptomic profiling in vascular diseases reveals systemic immune dysregulation." *Department of Biostatistics & Medical Informatics, University of Wisconsin, Madison, November 2012*

Poster Presentations

1. Sturek JM, Hedrick CC, Mauldin JP, **Huang CC**, Carr J, Swords-Jenny N, Goodarzi MO, Taylor K, Rotter JI, Adar SD, Kao WHL, Post WR, Danniel KR, Rick SS. ABCG1 SNPs, Diabetes, and Variation in Lipid Levels in the Multi-Ethnic Study of Atherosclerosis (MESA). *Joint Conference - 48th Cardiovascular Disease Epidemiology and Prevention -and- Nutrition, Physical Activity and Metabolism, Colorado Springs, CO, March 2008.*
2. Brown IJ, Elliott P, Chan Q, Daviglus ML,Dyer AR, **Huang CC**, Robertson CE, Rodriguez BL, Sakata K, Ueshima H, Van Horn L, Stamler J. Dietary Carbohydrate Intake of Individuals (Total, Starch, Total Sugar) and Their Blood Pressure: INTERMAP Study. *Joint Conference - 48th Cardiovascular Disease Epidemiology and Prevention -and- Nutrition, Physical Activity and metabolism, Colorado Springs, CO, March 2008.*
3. Gadd SL, **Huang CC**, Perlman EJ. Defining Subsets of Favorable Histology Wilms Tumor Using Global Gene Expression Analysis. *6th International Conference on the Biology of Childhood Renal Tumors, Chamonix-Mont Blanc, March 2008.*
4. Sredni ST, Gadd SL, **Huang CC**, Perlman EJ. Rhabdoid Tumors: Gene Expression Patterns ProvideClues to the Cell of Origin, Pathogenesis, and Potential Therapeutic Targets. *Thirteenth International Symposium on Pediatric Neuro-Oncology. Chicago, IL, July 2008.*
5. Sredni ST, Costa FF, **Huang CC**, Bonaldo MDF, Bischof J, Tomita T, Goldman S, Rajaram V, Soares MB. Study of Expression Pattern from 365 MicroRNAs in Atypical Theratoid-rhabdoid Tumors. A Comparison With Medulloblastomas. *40th Meeting of the International Society of Pediatric Oncology. Berlin, Germany, Oct 2008.*
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Candidate's Narrative Statement **June 2013**

Chiang-Ching Spencer Huang, PhD

Overview

I am submitting this narrative statement and accompanying materials in support of my request for tenure in the Joseph J. Zilber School of Public Health (ZSPH) at the University of Wisconsin-Milwaukee (UWM). Prior to my upcoming appointment beginning August 19, 2013 as an Associate Professor at the ZSPH, I have been an Associate Professor of Biostatistics and the Director of Bioinformatics Research Collaboratory at Northwestern University's Feinberg School of Medicine (FSM).

My primary research goals are to: 1) to employ modern genomics technologies and bioinformatics and biostatistics techniques to accurately predict risk for clinical and subclinical cardiovascular disease, and treatment response in cancer; and 2) to promote genomics and functional genomics research by providing strong state-of-the-art analytic and consultation support to the broader research community, in order to advance understanding of the major molecular mechanisms and pathways that modulate disease progression. My scholarly accomplishments while at Northwestern have led to increased recognition of my contributions to the fields of risk stratification and biomarker research using high-throughput "omics" technologies in cancer and cardiovascular disease. In addition, my academic contributions have been substantial in the areas of teaching, service, and national recognition.

Research

Cancer

In 2003 after receiving my PhD in biostatistics from the University of Michigan School of Public Health I joined the faculty at FSM, in the Department of Preventive Medicine, as an Assistant Professor. During the early days of microarray research, the mainstream biostatistical research direction was to identify differentially expressed genes or to develop classification algorithms for microarray gene expression data analysis. However, the lack of a biological context in this biostatistical investigation was a major limitation, and thus motivated me to combine genomics information with gene expression profiling data. My biostatistical methodology that applies the hidden-Markov-model to gene expression data becomes one of the pioneer works (CV Ref#15) in transcriptomic mapping to define expression patterns based on chromosomal locations and describe how abnormal expression patterns in specific chromosomal regions of cancer cells are associated with clinical outcomes.

In 2004, I assumed a leadership position as the subcontract principal investigator (PI) at Northwestern with Dr. Elizabeth Perlman, the chief pathologist at Children's Memorial Hospital in Chicago, in her NCI Director's Challenge project—"Categorization of Wilms' Tumor by Genetic Expression" (U01 CA088131). I analyzed more than 700 gene expression profiles of pediatric kidney tumors for the entire investigative team. The ultimate goal was to develop a molecular classification rule: 1) to identify patients with Wilms' tumor who do not respond to chemotherapy treatment; and 2) to accurately classify different types of pediatric kidney cancers to improve the current diagnostic system. Several milestone papers from this project have been published. The main results were published in a series of two papers: 1) the feature paper (CV Ref#13, first author) in *Pediatric Blood & Cancer*, the official Journal of the International Society of Paediatric Oncology (SIOP), documented a highly accurate molecular diagnostic signature that differentiates Wilms' tumor (WT), clear cell sarcoma of the kidney (CCSK), cellular mesoblastic nephroma (CMN), and rhabdoid tumor of the kidney (RTK); and 2) the largest Wilms' tumor microarray study published to date documented a significant improvement in prediction of treatment response by a gene expression signature (CV Ref#23, first author). We also discovered the systematic activation of the Sonic Hedgehog and Akt signaling Pathways in CCSK (CV Ref#12) and enhanced risk stratification for tumor recurrence by identifying a unique signature among patients who were thought to be in the very low risk Wilms' tumor (VLRWT) group by traditional criteria (CV Ref#25). Finally, we have used bioinformatics techniques to characterize the bivalent histone modification and polycomb group targets in embryonic stem cells in RTK (CV Ref#27). This body of work has contributed significantly to the

understanding of molecular characteristics in pediatric kidney cancers and suggested key molecular targets for therapeutic development to improve treatment efficacy.

Building upon the success of this initial Wilms' tumor project, Dr. Perlman and I were able to apply for the second phase of the NCI Director's Challenge initiative – Strategic Partnering to Evaluate Cancer Signatures (SPECS), and were awarded one of the six national projects: "Diagnostic and Prognostic Sarcoma Signatures" (U01 CA114757). The main aim of this project is to validate and refine previously identified gene signatures for Wilms' tumors and other non-soft tissue sarcomas to assess their diagnostic and prognostic utility. I served as the subcontract PI at Northwestern for this multi-institutional, multi-disciplinary collaborative project. This project was recently completed and several important findings have been presented at international/national conferences (CV poster presentations #3, #9, #10, #14). A paper in WT biology was recently published in 2012 (CV Ref#41, key bioinformatician) that identifies a subset of low-risk WT with a distinct molecular feature targets and suggests a revision of current model of WT ontogeny, which allows for an interplay between the type of initiating event and the developmental stage in which it occurs.

As high-throughput genomics technologies have evolved rapidly and there is a critical need to identify valid therapeutic targets in WT, Dr. Perlman and I further pursued research support to deepen the understanding of molecular mechanisms in high-risk anaplastic WT. We were funded again for our application, "Analysis of High Risk Wilms' Tumor" (U10 CA98543), through another NCI initiative—The Therapeutically Applicable Research to Generate Effective Treatments (TARGET). The challenge of this new project is daunting because the analysis of massive whole-genome next-generation sequencing data and its integration with other genome-wide mRNA/microRNA expression and methylation data require enormous bioinformatics input and collaborative effort. Recognizing the complexity of this project, I organized a strong bioinformatics team including faculty and research fellows in the Bioinformatics Core of the Lurie Cancer Center to support this project that has a high demand for intensive data analysis. I serve as the subcontract PI at Northwestern on this intensive project.

Cardiovascular Diseases

Since joining Northwestern I have been provided with constant exposure to the most up-to-date CVD epidemiological research. Through my contact with colleagues in the Department of Preventive Medicine, I came to realize that the current paradigm of risk prediction for CVD using conventional risk factors such as cholesterol, blood pressure, and smoking needs improvement. Although several blood biomarkers have been proposed to identify high-risk populations, none of them has been incorporated into clinical practice. To overcome this bottleneck in biomarker research that is largely attributable to the complexity and heterogeneity of CVD, I decided to apply my substantial experience in cancer molecular and bioinformatics research to address this CVD risk prediction question. In 2007, I received funding for my R01 (with a priority score at the 2nd percentile) that has allowed me to investigate the molecular mechanisms associated with development of advanced atherosclerosis among apparently healthy women with a low burden of traditional CVD risk factors. This innovative project is a pioneering study in CVD research to refine CVD risk prediction using whole-genome microarray gene expression profiling. The goal of the study was to construct a multi-gene classification rule and identify molecular signaling pathways that can distinguish asymptomatic women with and without subclinical atherosclerosis. To date, the Framingham risk score (FRS) has been the gold standard for 10-year coronary heart disease risk prediction. However, a substantial proportion of individuals with low to intermediate FRS, i.e., FRS<20%, still develop atherosclerosis, and go on to have fatal and non-fatal CVD events as a result. I based this study within the pre-existing cohort of the Multi-Ethnic Study of Atherosclerosis (MESA) (an ongoing NHLBI-funded longitudinal cohort study which has a clinical center at Northwestern, PI: Kiang Liu, PhD). After extensive efforts to collect blood samples from 119 carefully selected female participants (48 low-risk women with substantial burden of atherosclerosis and 71 low-risk controls without atherosclerosis), I focused on the integration of whole-genome expression data with a broad array of MESA phenotypic data. This effort required extensive bioinformatics and biostatistical analyses, and the

comparison of our data with other microarray studies on the inflammatory condition. We discovered that, compared with controls, there is a systematic activation of toll-like receptor (TLR) signaling pathways, the key pathway in the innate immune system, in low-risk women who nonetheless have a significant burden of subclinical atherosclerosis (odds ratio 5.3, 95% CI=[2.3, 12.4]). This translational finding is significant in several ways. First, it supports the involvement of TLR signaling in the initiation and progression of atherosclerosis that has been reported from several lines of experimental and animal studies. Second, it highlights an important molecular link between atherosclerosis and autoimmune diseases such as lupus and rheumatoid arthritis (RA), because TLR signaling has been implicated in these diseases and individuals with autoimmune diseases have a two- to three-fold increased risk of developing atherosclerosis compared to the general population. This work was presented at the annual American Heart Association (AHA) Scientific Meeting (2008) and received the best poster award in the Population Science Session. This proof-of-principle study is the first report to demonstrate the feasibility of using whole-genome expression profiling technologies to refine CVD risk assessment among a low-risk population. The paper was recently published in *PLoS ONE* (CV Ref#34, first and corresponding author). Further exploration of the utility of this methodology for clinical risk prediction, and validation/ replication studies, are being planned.

The data generated by this project have allowed further insights into disease mechanisms. Epidemiologic studies have shown that coronary artery calcium (CAC) is highly correlated with the burden of atherosclerosis and is an independent risk factor for CVD. Several studies have shown that African Americans have a significantly lower prevalence of CAC and average CAC score than whites, despite a higher prevalence of hypertension and diabetes. Nevertheless, the mechanisms accounting for the differential CAC burden between whites and African Americans are poorly understood. Underlying biological processes and genetic predisposition are likely to play a role in the modulation of CAC. In light of the potential to further understand atherogenesis, I pursued this scientific inquiry by analyzing and comparing the gene expression patterns between these two populations. I found that not only was there a significant and substantial difference in the global gene expression patterns between whites and African Americans, but a substantial number of differentially expressed genes were associated with atherosclerosis and were involved in calcium mobilization and the immune/inflammatory response. More importantly, genetic variation between these two populations is attributable to expression differences of 50% of race-associated genes. This novel finding suggests that studying gene expression variation among populations can provide insight into disease etiology. This research has led me to a new research direction that will be described later. This work was presented (as an oral abstract) at the AHA Joint Conference on Cardiovascular Disease Epidemiology and Prevention and Nutrition, Physical Activity and Metabolism (March, 2011) and the manuscript was published in *Physiological Genomics* as a feature paper (CV Ref #35, first and corresponding author).

Autoimmune Diseases

Because of my expertise in gene expression profiling studies, I was invited to join a research endeavor in the Department of Medicine, Division of Rheumatology. Specifically, in 2007, I assisted Dr. Rosalind Ramsey-Goldman, Solovy Arthritis Research Society Professor, with her microarray gene expression project -- SOLVABLE: Study of Lupus Vascular and Bone Long-term Endpoints. The goal of this project is to identify gene expression signatures in order to understand the development of the complications of osteoporosis and cardiovascular disease in systemic lupus erythematosus (SLE). This project was one of the funded center research projects in the NIH/NIAMS-funded "Multidisciplinary Clinical Research Center in Rheumatology" (PI: Dr. Richard Pope) at Northwestern. The microarray gene expression data for monocytes and macrophages were recently analyzed from SLE patients and healthy controls, showing an interferon-inducible gene signature in about 50% of lupus patients. Furthermore, the TLR signature identified in my MESA study was strongly associated (odds ratio 9.3, 95% CI= [1.2, 72.9]) with atherosclerosis among the lupus patients and also may be associated with SLE (odds ratio 7.0, 95% CI= [0.86, 56.9]). These results suggest that TLR is a common molecular link between SLE and

atherosclerosis and may explain why SLE patients develop atherosclerosis at a much younger age than the general population. This work was presented in the American College of Rheumatology (ACR) 2011 Annual Scientific Meeting (CV poster presentation #18) and the manuscript was recently submitted to *Arthritis & Rheumatism* and is under review.

In summary, I view my role as one in which I perform important functions as a principal investigator, but also as a key collaborator helping other investigators with the biostatistical and bioinformatics methods needed to interpret the vast array of data generated in –omics studies. I thus serve an increasingly important "connector" function among molecular geneticists, classical epidemiologists and clinicians.

Future Directions in Research

New Directions in Risk Prediction and Biomarker Discovery using Metabolomics

My initial work in functional genomics, and specifically gene-expression profiling, helped me realize that the end-products of gene transcription, translation and protein processing can also be useful biomarkers. These end-products typically are small molecules and are commonly referred to as "metabolites"; they are the downstream molecules that result from the complex interaction between host genome and environment, and hence may be the best reporter of an individual's physiological status. I have collaborated with Dr. Jane Tseng, Director of the Metabolomics Core at National Taiwan University, on several metabolomic pilot projects during the past three years. Because of the rich resources of several large and unique CVD population and clinical cohorts at Northwestern, I will continue to collaborate with Dr. Tseng and my FSM colleagues to understand how metabolism measured by "metabolomics" influences an individual's susceptibility to chronic diseases after joining UWM. I am planning an R21 application to investigate how lipid metabolites influence TLR/IL1B signaling in atherosclerosis. The goal of this exploratory research is to utilize state-of-the-art mass-based lipidomics technology for unbiased identification of novel lipids, especially oxidized phospholipids, that may inhibit TLR/IL1B signaling in atherosclerosis, thereby providing a potential therapeutic target for prevention. Dr. Tseng from the National Taiwan University had a very generous offer last December (2012) to perform metabolomics and lipidomics experiments on all the 1,400 participants' stored plasma samples from the Northwestern-based cohort study, the Chicago Health Aging Study (CHAS, PI: Dr. Martha Daviglus). With this one of the largest international metabolomics collaborations, the comprehensive metabolomics and lipidomics data along with the rich phenotype data in CHAS not only can address the relation between TLR/IL1B signaling and oxidized phospholipids, but also provide an unprecedented opportunity to systematically investigate important biomedical questions such as how metabolism influences pathophysiological status, especially frailty among the older population. I anticipate this data will open up many opportunities for grant application in biomarker research in the coming years. We recently discovered a lipid metabolite signature that can robustly predict near-term all-cause death among individuals with peripheral artery diseases (PAD) (CV Ref#44, first author). This finding has significant implications for researchers and clinicians seeking to identify high risk patients for intervention. An R01 grant application is under planning to further refine this metabolite signature in a larger PAD cohort.

The knowledge gained from my previous gene expression work in atherosclerosis as well as SLE has inspired my future population research. First, several lines of research have shown that autoimmune diseases (i.e., lupus, rheumatoid arthritis (RA), multiple scleroderma (MS), type I diabetes) and type II diabetes are associated with an increased risk of atherosclerosis. Although inflammation seems to be a common mechanism, the molecular pathways leading to systemic inflammation may be diverse among these diseases. Second, the prevalence of the aforementioned diseases is substantially different among different ethnic groups. Although life style, dietary pattern, and socio-economic status are all important factors, genetic variation between ethnic groups undoubtedly plays a major role in such disparities. In light of these population observations, I will continue to collaborate with FSM-based investigators, and potentially opportunities in UWM, Aurora Heath Care, and Medical College of Wisconsin to take

advantage of several well-phenotyped national and local population/clinical cohorts in CVD, RA, SLE, and MS to perform a systematic investigation of the dynamic molecular phenotype of these diseases and populations. This innovative and exciting research direction has the potential to unveil the multiple underlying molecular pathways leading to the manifestation of atherosclerosis. Combining information from these signaling pathways will be a breakthrough in biomarker research and thereby enhance the power of risk prediction for atherosclerosis. This approach, if successful, will provide a holistic and integrative strategy to refine risk assessment and target therapy for atherosclerosis, the leading cause of morbidity and mortality in the world.

Systems Biology in Population and Clinical Study

My research has been focused on using novel technologies and bioinformatics techniques to tackle challenging biomedical problems. Microarray gene expression profiling is a powerful tool; however, my recent exposure to other high-throughput -omics data (i.e., epigenome, metabolome, and next generation sequencing) has suggested new avenues for the application of systems biology in population and clinical research. The results from integration of various -omics data have challenged several biological principles and our knowledge of molecular control is evolving. Therefore, how to translate or discover new biological information to address important clinical questions will be my next research agenda. With my extensive experience and research involvement in biostatistics, epidemiology, bioinformatics, CVD, cancer, and autoimmune disease, I will bring innovation and creativity into the School of Public Health and the broader UWM research community.

Teaching Activities

Mentoring. I am most proud of my role as a research mentor for junior faculty outside the Department and for Master of Science in Epidemiology and Biostatistics (MSEB) students in our Department. This aspect of my faculty responsibility has also become one of the most rewarding. I have played a major role (see below) in mentoring two junior faculty members in their promotion, peer-reviewed publications, and grant funding. I served as the primary mentor on Dr. Simone Sredni, a then-research associate at Children's Memorial Hospital, to secure her first research grant to study the epigenetic instability of malignant rhabdoid tumors, funded by the Rally Foundation for Childhood Cancer Research (2009-2011). Because of the success of this study, I continued to guide her to obtain her second Rally Foundation grant to investigate diagnostic markers and new therapeutic targets in undifferentiated sarcomas in children (2011-2013). This research accomplishment also helped her to be promoted to research assistant professor effective January 2011. My other mentee is Dr. Monique Hinchcliff, who was promoted to Assistant Professor of Medicine in the Division of Rheumatology in September 2010. I have been her primary bioinformatics mentor in genomics and biomarker research in scleroderma. I was instrumental in her Scleroderma Foundation grant funding that began in July 2011. This project aims to identify a gene signature of skin biopsies from patients with systemic sclerosis (SSc) that can predict clinical response to mycophenolate mofetil (MMF), the most common drug used for SSc. This work was recently published in *Journal of Investigative Dermatology* (CV Ref#42). I regularly meet with Dr. Hinchcliff to guide her in manuscript preparation, grant preparation, and how to use novel genomics technologies to perform translational research in scleroderma. I firmly believe that my mentoring contributions have helped to foster a new generation of biomarker and genomics researchers.

Teaching. Since joining the faculty at Northwestern in September 2003, I have been actively involved in teaching MSEB students and MSCI (MS in Clinical Investigation) students at FSM, and students in the Department of Statistics (from the Evanston Campus). I have participated in lectures in courses for bioinformatics and computational biology in the Department of Statistics from 2003 to 2005. When the new MSEB program in Preventive Medicine was approved by Northwestern's graduate school in 2006, I developed a new biostatistics course, "Statistical Consultation" (EPI BIO 499), to sharpen students' skills in data analysis and interpretation of real-world case studies; this course has since become one of the core courses in this program's curriculum. In 2008, I was invited to give a summer course, "Bioinformatics

Using R", at National Taiwan University, the leading research university in Taiwan. After this teaching experience, I had a strong desire to teach a similar course in our MSEB program because this course is critical in modern biomedical research and enables our master's degree graduates to be more competitive in the job market. Therefore, I developed and offered a new course, "Bioinformatics and Data Mining" (EPI BIO 428) – in winter quarter 2011. This course combined theory and real-world applications so that students not only learned how to use modern statistical techniques to analyze large-scale genomics data, but also developed an appreciation for modern genomics technologies in advancing medical research. This course received very positive feedback from the students (see Course Evaluation).

I plan to develop a concentrated curriculum—"Bioinformatics in Population Science" – in the coming years when I join UWM. This curriculum will include a series of courses in computational biology, biomedical informatics, and epidemiology. The ultimate goal of this curriculum is to train and prepare students to become next-generation biostatisticians/epidemiologists and facilitate multidisciplinary collaborations as a result of increasing teaching interactions among faculty members.

International, National, and Regional Societies/Meetings and Other Invited Lectures. As noted on my CV, I have given several invited lectures at regional, national, and international meetings over the last nine years. As part of these activities, I have spoken at national meetings in China, France, and the United States, and have given invited lectures or short courses at institutions in Taiwan and the United States, mainly on the topics related to bioinformatics, personalized medicine, and functional genomics.

Service

For the MSEB, I have served on the Evaluation Committee and I have been an ad hoc member for the thesis committee in the MSEB program. I also am a member of the Center for Genetic Medicine and provide input and consultation to Center members for omics study design and data analysis. I plan to serve on other School and University committees in the coming years in UWM. For national and international service, I have served on the Genetics Committee in MESA (since 2007) and CARDIA (since 2008) and I review manuscript proposals and manuscript drafts on a regular basis. I also served as an ad hoc member of a grant review committee (NIH/NIGMS) for a RC2 Grand Opportunities (GO) application and Taiwan National Health Research Institutes extramural grant scientific review this year. I have served as an ad hoc reviewer for several medical journals such as *JAMA, Circulation, Journal of Proteome Research, Bioinformatics.* In 2010, I was invited to serve on the scientific program committee of the International Chinese Statistical Association (ICSA) and organized an invited session, "Statistical Issues in Analyzing Emerging Genomic Data", for the annual ICSA meeting in Indianapolis. As a result of my work in atherosclerosis risk refinement and biomarker discovery, I was invited to present my research on CVD and organize a scientific session titled "Coronary Artery Disease Risk Factors" for the 3rd Annual International Congress of Cardiology (Beijing, 2011).

Thus, I have laid a solid foundation in my research that is an excellent combination of innovation and practical application. I am increasingly being recognized as an innovative, pioneering researcher and a key collaborator in my field of bioinformatics and CVD/cancer risk stratification using novel genomics technologies. While continuing to support the bioinformatics and biostatistics needs of the research community, the trajectory of my research, teaching, original publications, and service has been extremely positive, and suggests that I will continue to make important contributions while advancing in my career path in the coming years.