BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Wang, Kai.

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

POSITION TITLE: Professor

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
Lanzhou University, Lanzhou, Gansu	ВА	07/1986	Mathematics
Nankai University, Tianjin	MA	07/1989	Econometrics
University of Iowa, Iowa City, Iowa	MS	05/1996	Economics
University of Iowa, Iowa City, IA	PHD	12/1999	Statistics

A. Personal Statement

B. Positions and Honors

Positions and Employment

1999 - 1999	Research Assistant Professor, Medical Statistics Section, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL
1999 - 1999	Biostatistician, Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL
1999 - 2003	Assistant Professor, Department of Biostatistics, College of Public Health, University of Iowa, Iowa City, IA
2003 - 2005	Assistant Professor, Program in Public Health Genetics, College of Public Health, University of Iowa, Iowa City, IA
2005 - 2007	Associate Professor, Program in Public Health Genetics, College of Public Health, University of Iowa, Iowa City, IA
2007 - 2013	Associate Professor, Department of Biostatistics, College of Public Health, University of Iowa, Iowa City, IA
2010 - 2013	Associate Professor, Interdisciplinary Graduate Degree Program in Informatics, Bioinformatics Subtrack, University of Iowa, Iowa City, IA
2013 -	Professor, Department of Biostatistics, College of Public Health, University of Iowa, Iowa City, IA

Other Experience and Professional Memberships

2002 -	Member, International Genetic Epidemiology Society
2011 -	Member, American Statistical Association (ASA)
2011 -	Member, International Biometric Society (ENAR)

C. Contributions to Science

- With the rapid development of high throughput biological technology, unprecedented amount of data are available for gene mapping studies. Such data raise new challenges to statistical analysis. I have developed new statistical methods for multipoint genetic linkage analysis, robust statistics for genetic association analysis, gene-based association methods, and high-dimensional data analysis.
 - a. Wang K. Boosting the Power of the Sequence Kernel Association Test by Properly Estimating Its Null Distribution. Am J Hum Genet. 2016 Jul 7;99(1):104-14. PubMed PMID: <u>27292111</u>; PubMed Central PMCID: <u>PMC5005443</u>.
 - b. Huang J, Wang K, Wei P, Liu X, Liu X, Tan K, Boerwinkle E, Potash JB, Han S. FLAGS: A Flexible and Adaptive Association Test for Gene Sets Using Summary Statistics. Genetics. 2016 Mar;202(3):919-29. PubMed PMID: 26773050; PubMed Central PMCID: PMC4788129.
 - c. Wang K, Abbott D. A principal components regression approach to multilocus genetic association studies. Genet Epidemiol. 2008 Feb;32(2):108-18. PubMed PMID: <u>17849491</u>.
 - d. Wang K, Sheffield VC. A constrained-likelihood approach to marker-trait association studies. Am J Hum Genet. 2005 Nov;77(5):768-80. PubMed PMID: <u>16252237</u>; PubMed Central PMCID: <u>PMC1271386</u>.
- 2. Polychlorinated biphenyls (PCB) is a large family of environmental pollutants that cause many different types of adverse human health effects including cancer. I have been serving the role of statistician for the lowa Superfund Research Program for 9 years. Our research results are essential for risk assessment, development of strategies to prevent or ameliorate toxicity, and for management of these toxicants in human environments.
 - a. Wang B, Klaren WD, Wels BR, Simmons DL, Olivier AK, Wang K, Robertson LW, Ludewig G. Dietary Manganese Modulates PCB126 Toxicity, Metal Status, and MnSOD in the Rat. Toxicol Sci. 2016 Mar;150(1):15-26. PubMed PMID: 26660635; PubMed Central PMCID: PMC5009614.
 - b. Koh WX, Hornbuckle KC, Marek RF, Wang K, Thorne PS. Hydroxylated polychlorinated biphenyls in human sera from adolescents and their mothers living in two U.S. Midwestern communities. Chemosphere. 2016 Mar;147:389-95. PubMed PMID: <u>26774304</u>; PubMed Central PMCID: <u>PMC4747419</u>.
 - c. Lai IK, Klaren WD, Li M, Wels B, Simmons DL, Olivier AK, Haschek WM, Wang K, Ludewig G, Robertson LW. Does dietary copper supplementation enhance or diminish PCB126 toxicity in the rodent liver?. Chem Res Toxicol. 2013 May 20;26(5):634-44. PubMed PMID: 23527585; PubMed Central PMCID: PMC3660509.
 - d. Marek RF, Thorne PS, Wang K, Dewall J, Hornbuckle KC. PCBs and OH-PCBs in serum from children and mothers in urban and rural U.S. communities. Environ Sci Technol. 2013 Apr 2;47(7):3353-61. PubMed PMID: 23452180; PubMed Central PMCID: PMC3645264.
- 3. Primary open angle glaucoma (POAG) and age-related macular degeneration are leading causes of blindness worldwide. I have been involved in genetic analysis on these two phenotypes for more than 10 years. Our studies has made a number of findings, including novel mutations in ABCA4 gene. These findings are being used for genetic testing at the The Stephen A. Wynn Institute for Vision Research at the University of Iowa
 - a. Hedberg-Buenz A, Christopher MA, Lewis CJ, Fernandes KA, Dutca LM, Wang K, Scheetz TE, Abràmoff MD, Libby RT, Garvin MK, Anderson MG. Quantitative measurement of retinal ganglion cell populations via histology-based random forest classification. Exp Eye Res. 2016 May;146:370-85. PubMed PMID: <u>26474494</u>; PubMed Central PMCID: <u>PMC4841761</u>.
 - b. Stunkel M, Bhattarai S, Kemerley A, Stone EM, Wang K, Mullins RF, Drack AV. Vitritis in pediatric genetic retinal disorders. Ophthalmology. 2015 Jan;122(1):192-9. PubMed PMID: <u>25217415</u>; PubMed Central PMCID: <u>PMC4277925</u>.
 - c. Sohn EH, Wang K, Thompson S, Riker MJ, Hoffmann JM, Stone EM, Mullins RF. Comparison of drusen and modifying genes in autosomal dominant radial drusen and age-related macular degeneration. Retina. 2015 Jan;35(1):48-57. PubMed PMID: <u>25077532</u>.
 - d. Mullins RF, Schoo DP, Sohn EH, Flamme-Wiese MJ, Workamelahu G, Johnston RM, Wang K, Tucker BA, Stone EM. The membrane attack complex in aging human choriocapillaris: relationship to macular degeneration and choroidal thinning. Am J Pathol. 2014 Nov;184(11):3142-53. PubMed PMID: 25204844; PubMed Central PMCID: PMC4215023.

- 4. Many blood disorders are due to genetics. I have conducted genetic analysis on a number projects related to blood disorders. These studies lead to a finding that mutations in NBEAL2 gene associated with gray platelet syndrome, a confirmation of 3p21 as a recessive locus for gray platelet syndrome, and some novel candidate loci for erythrocyte traits.
 - a. Fabbro S, Kahr WH, Hinckley J, Wang K, Moseley J, Ryu GY, Nixon B, White JG, Bair T, Schutte B, Di Paola J. Homozygosity mapping with SNP arrays confirms 3p21 as a recessive locus for gray platelet syndrome and narrows the interval significantly. Blood. 2011 Mar 24;117(12):3430-4. PubMed PMID: <a href="https://doi.org/10.103/enable-1
 - b. Kahr WH, Hinckley J, Li L, Schwertz H, Christensen H, Rowley JW, Pluthero FG, Urban D, Fabbro S, Nixon B, Gadzinski R, Storck M, Wang K, Ryu GY, Jobe SM, Schutte BC, Moseley J, Loughran NB, Parkinson J, Weyrich AS, Di Paola J. Mutations in NBEAL2, encoding a BEACH protein, cause gray platelet syndrome. Nat Genet. 2011 Jul 17;43(8):738-40. PubMed PMID: 21765413.
 - c. Hinckley JD, Abbott D, Burns TL, Heiman M, Shapiro AD, Wang K, Di Paola J. Quantitative trait locus linkage analysis in a large Amish pedigree identifies novel candidate loci for erythrocyte traits. Mol Genet Genomic Med. 2013 Sep 1;1(3):131-141. PubMed PMID: <u>24058921</u>; PubMed Central PMCID: <u>PMC3775389</u>.
 - d. Gonzalez-Alegre P, Di Paola J, Wang K, Fabbro S, Yu HC, Shaikh TH, Darbro BW, Bassuk AG. Evaluating Familial Essential Tremor with Novel Genetic Approaches: Is it a Genotyping or Phenotyping Issue?. Tremor Other Hyperkinet Mov (N Y). 2014 Oct 20;4:258. PubMed PMID: <u>25374765</u>; PubMed Central PMCID: <u>PMC4219111</u>.
- 5. I have been participating in a number of other projects. These projects include studies on Bardet-Biedl Syndrome, cystic fibrosis, atypical hemolytic uremic syndrome, idiopathic scoliosis, and epigenetic markers for smoking.
 - a. Mondal P, Baumstein S, Prabhakaran S, Abu-Hasan M, Zeng Y, Singh S, Wang K, Ahrens RC, Hendeles L. Bioassay of salmeterol in children using methacholine challenge with impulse oscillometry. Pediatr Pulmonol. 2016 Jun;51(6):570-5. PubMed PMID: 26575323.
 - b. Fisher JT, Tyler SR, Zhang Y, Lee BJ, Liu X, Sun X, Sui H, Liang B, Luo M, Xie W, Yi Y, Zhou W, Song Y, Keiser N, Wang K, de Jonge HR, Engelhardt JF. Bioelectric characterization of epithelia from neonatal CFTR knockout ferrets. Am J Respir Cell Mol Biol. 2013 Nov;49(5):837-44. PubMed PMID: <u>23782101</u>; PubMed Central PMCID: PMC3931095.
 - c. Seo S, Mullins RF, Dumitrescu AV, Bhattarai S, Gratie D, Wang K, Stone EM, Sheffield V, Drack AV. Subretinal gene therapy of mice with Bardet-Biedl syndrome type 1. Invest Ophthalmol Vis Sci. 2013 Sep 11;54(9):6118-32. PubMed PMID: 23900607; PubMed Central PMCID: PMC3771708.
 - d. Gonzalez-Alegre P, Buffard V, Wang K, Henien S, Morcuende JA. Exploring the link between dystonia genes and idiopathic scoliosis. J Pediatr Orthop. 2013 Sep;33(6):e65-6. PubMed PMID: 23812140.

Complete List of Published Work in My Bibliography: http://bit.ly/2jDnWMw

D. Additional Information: Research Support and/or Scholastic Performance

Current Research

R01 ES022163 (Rohlman, Diane, Pl) 03/04/13-10/31/19

NIH

Vulnerability of the Adolescent Brain to Organophosphorus Pesticides

Despite evidence from human and animal studies that clearly identifies neurotoxicity as the primary adverse endpoint, the long-term effects of repeated occupational and environmental exposures to organophosphorus pesticides (OPs) remain poorly understood. There is also a critical need to investigate the susceptibility of children and adolescents to pesticides, since the developing brain may be uniquely sensitive to the neurotoxic effects of these agents. We propose a longitudinal study to investigate the relationship between sensitive and specific biomarkers of pesticide exposure, effect and susceptibility and multiple measures of neurobehavioral function in this unique cohort over a 5-year period to assess cumulative and potentially reversible effects.

Role: Co-Investigator

P42 ES013661 (Robertson, Larry ,PI) 05/12/2006-03/31/2020

NIH/NIEHS

Semi-Volatile PCBs: Sources, Exposures, Toxicities (Superfund Research Program Administrative Core)

The Administrative Core is the focal point for the Research Projects and Cores of the Iowa Superfund Research Program and provides administrative oversight, statistical consulting, research results reporting, and serves as a liaison between the stakeholders, University officials, and the SRP.

Role: Co-Investigator

R24 DK096518 (Engelhardt, John, PI) 08/15/2012-06/30/2019

NIH

Early Pathogenesis of Cystic Fibrosis Related Diabetes

Cystic Fibrosis (CF) is the most common life-threatening autosomal recessive condition among Caucasians, with over \$450 million dollars spent annually on clinical care of CF patients in the U.S. alone. Cystic fibrosis related diabetes (CFRD) is the most common severe complication of CF and is well known to be associated with increased mortality and a decline in lung function. This study will characterize early disease mechanisms that lead to the development of CFRD in animal models and humans, with the long-term goal of developing improved therapies and biomarkers for early diagnosis and treatment of this disease.

Role: Biostatistician

R01 DC002842 (Smith, Richard, PI) 09/30/96-08/31/2019

NIH

Non-Syndromic Hearing Loss - A Collaborative Study

The identification of ARNSD genes lead to the development of novel therapies to treat deafness; the ability to recognize specific types of genetic deafness has made comparative studies of genotype, phenotype and habilitative outcome feasible; and the use of genetic testing to diagnose many types of ARNSD has changed the medical evaluation of the deaf person. This grant will continue to focus on these three areas by completing specific aims: 1) to identify novel ARNSD genes; 2) to define genotype-phenotype associations in persons with DFNB1 deafness; 3) to study Pendred syndrome as a complex disease, focusing on the role of FOXI1 and its interacting partners in the Pendred syndrome phenotype.

Role: Co-Investigator

R01 HG008348 (Klein, David, PI) 08/10/2015-05/31/2019

NIH

Interactive Multimedia Consent for Biobanking

To support next-generation genomic research and science, many biobanks in the U.S. consent thousands of contributors of biospecimens and health information. There is growing interest in the efficiency of electronic consenting (e-consent) given the scale of these efforts. The long-term objective of this three-year (R01) study is to improve the efficiency and effectiveness of informed consent through use of systematically developed e-consent tools. Overall, the study is expected to contribute to ethical, cost-effective genomic research recruitment efforts through in-depth empirical knowledge of IM consenting technology.

Role: Co-Investigator

R01 EY026087 (Stone, Ed, PI) 09/01/2016-08/31/2020

NIH

Unraveling the 10q AMD Risk Locus

In this study, we will take advantage of molecular genetics, state of the art computer-assisted image analysis, large patient populations, donor eye tissue, induced pluripotent stem cells and CRISPR based genome editing to determine the molecular mechanism through which variations at the 10q AMD locus increase the risk of AMD.

Role: Co-Investigator

P30 ES005605 (Thorne, Peter, PI) 09/29/90-03/31/22

NIH

Environmental Health Sciences Research Center

Building on a 26-year history, the Environmental Health Sciences Research Center (EHSRC) will advance and translate cutting edge research that addresses environmental health problems across the urban-rural continuum. The EHSRC vision is to be the primary environmental health sciences (EHS) resource for improving the health of rural residents by stimulating and translating innovative EHS research. Center goals are to: 1) Develop, support and expand innovative interdisciplinary EHS research in key Thematic Areas; 2) Recruit, mentor and nurture talented new and mid-level investigators in EHS; and 3) Engage with communities and policy makers to translate research findings toward improving the health and environment of rural people in the Midwest and the nation.

Role: Co-Investigator

R21 HD091458 (Bao, Wei) 07/10/17-06/30/19

NIH

Pregnancy-Associated microRNAs in Plasma as Predictors of Gestational Diabetes

Role: Co-Investigator

R21 ES027169 (Lehmler, Hans-Joachim) 09/01/17-08/31/19

NIH

PCB Enantiomers Implicated in Neurodevelopmental Disorders: Identification of Individual Metabolic Factors that Determine Risk and Vulnerability

The long-term goal of this project is to determine how inter-individual differences in enantioselective PCB metabolism affect the susceptibility to PCB-mediated neurodevelopmental disorders following environmental exposures and, ultimately, reduce the burden of these diseases.

Role: Co-Investigator

Completed Research

R01 EY017673 (Anderson, Michael Gary, PI) 04/01/2008-01/31/2018

NIH

Genetic Dissection of Pigmentary Glaucoma

Glaucoma is a leading cause of irreversible blindness and visual disability that has a major impact on the quality of life and productivity of millions of Americans. With no new pharmaceutical classes for treating glaucoma introduced into clinical practice since the 1990s, there remains a continuing need for improved regimes that treat glaucoma more effectively. Our long-term goal is to contribute to the development of these improved therapies by utilizing synergistic genetic approaches with mice and humans. Our objective in this proposal is to utilize and build on these resources to study molecular events contributing to pigment dispersion and its conversion to pigmentary glaucoma. To accomplish this, we propose: (SA1) to identify suppressors of pigmentary glaucoma using hereditary mouse models, (SA2) to define predictors of ocular responses to pigment dispersion using inducible mouse models, and (SA3) to identify genes linked with pigmentary glaucoma using human patient cohorts.

Role: Co-Investigator