BIOGRAPHICAL SKETCH

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NAME: Guo, Shicheng, PhD

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

POSITION TITLE:

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Northeast Agricultural University, Harbin, China	B.S.	06/2009	Biology
Fudan University, Shanghai, China	Ph.D.	01/2015	Human Genetics
University of Texas Health Science Center at Houston, Houston, TX	Postdoc	04/2015	Genetic Epidemiology
University of California, San Diego, CA	Postdoc	10/2017	Human Genetics

A. Personal Statement

My research has focused on the development and analysis of the epigenomic architecture assembly of human cells/tissue and other important model organisms using epigenetic- (DNA methylation and miRNA profiles) and genetic variant- (single-nucleotide polymorphisms (SNPs) and copy number variant (CNV) screens) based approaches. Through this work, I have discovered susceptibility factors associated with the development and progression of various diseases. These disease-susceptibility factors can be used as diagnostic and prognostic biomarkers to further clinical research in human complex diseases, such as lung cancers, thyroid cancer, bladder cancer, liver cancer, ankylosing spondylitis (AS), gout, and systemic sclerosis (SSc). My previous work includes (i) the identification of SSc and RA-predisposing SNPs and CNVs using case-control approaches, (ii) identification of diagnostic biomarkers for solid tissue human cancers, and (iii) origin-tissue mapping for cell-free DNA based on tissue-specific methylation panels. Current areas of investigation include disease susceptibility screening using genome-wide association studies (GWAS) and phenome-wide association studies (PheWAS) approaches and assessing the genetic-epigenetic interactions in the identification, etiology, and treatment of various human diseases. The ultimate goal of my research is to develop widely-applicable biomarker-based methods for disease diagnosis, disease subtype identification, and/or prognosis. I have experience with different bioinformatics-based analyses for genetic variation, epigenetic data (methylation sequencing, ChIP-seq data), text-mining, and machine learning analysis using Perl, R, and Python programs which will serve me well in a broad array of projects utilizing bioinformatics and biostatistics analyses.

B. Positions and Honors

Positions and Employment

2015-2015 Postdoctoral Fellow, University of Texas Health Science Center at Houston, TX
2015-2017 Postdoctoral Fellow, University of California, San Diego, CA
2017-Present Postdoctoral Fellow, Center for Human Genetics, Marshfield Clinic, WI

Other Experience and Professional Memberships

2011-2014 Internship, Institute of Rheumatology, Immunology and Allergy, Shanghai, China
2012-2013 Internship, CAS-MPG Partner Institute for Computational Biology, Shanghai, China
2012-2013 Visiting Scholar, University of Texas Health Science Center at Houston, Houston, TX
2013-2015 Research Assistant, University of Texas Health Science Center at Houston, Houston, TX

Honors

2007 Second prize of National Mathematical Modeling Contest in Heilongjiang province, Harbin, China
2012 Silver award of "Cup of Challenge" for College Students' Innovative Undertaking Contest, Shanghai
2014 First Place Poster, 17th Annual Human and Molecular Genetics Program Symposium, GSBS, TX

C. Contribution to Science

1. Identification of autoimmune disease susceptibility genetics

Early in my career, I investigated genetic variants involved in systemic sclerosis (SSc) and rheumatoid arthritis within the Chinese Han population. Applying a multiple candidate pre-selection method (SNP and CNV screens), I identified multiple susceptibility genes, such as an important CNV within *HLA-DQA1* and *APOBEC3A/3B* for SSc, *CFH* for age-related macular degeneration, and *FOXE1* for thyroid cancer. I also conducted a large association study interrogating genetic variants in miRNA for human cancer and identified miR-4293 as being significantly associated with non-small cell lung cancer, and miR-196a2/miR-499 involved in esophageal squamous cell carcinoma. These findings have provided much needed molecular insight into the role of miRNA regulation and genetic variants involved in these cancer etiologies.

a. Huang, L[‡], Y. Li[‡], **S. Guo**[‡], Y. Sun, C. Zhang, Y. Bai, S. Li, F. Yang, M. Zhao, B. Wang, W. Yu, C.C. Khor, and X. Li, Different hereditary contribution of the CFH gene between polypoidal choroidal vasculopathy and age-related macular degeneration in Chinese Han people. Invest Ophthalmol Vis Sci, 2014. 55(4): p. 2534-8. ([‡]Contributed equally)
b. Shen, F., J. Chen, **S. Guo**, Y. Zhou, Y. Zheng, Y. Yang, J. Zhang, X. Wang, C. Wang, D. Zhao, M. Wang, M. Zhu, L. Fan, J. Xiang, Y. Xia, Q. Wei, L. Jin, and J. Wang, Genetic variants in miR-196a2 and miR-499 are associated with susceptibility to esophageal squamous cell carcinoma in Chinese Han population. Tumour Biol, 2016. 37(4): p. 4777-84.
c. **Guo, S**., Y. Li, Y. Wang, H. Chu, Y. Chen, Q. Liu, G. Guo, W. Tu, W. Wu, H. Zou, L. Yang, R. Xiao, Y. Ma, F. Zhang, M. Xiong, L. Jin, X. Zhou, and J. Wang, Copy Number Variation of HLA-DQA1 and APOBEC3A/3B Contribute to the Susceptibility of Systemic Sclerosis in the Chinese Han Population. J Rheumatol, 2016. 43(5): p. 880-6.
d. **Guo, S**[‡], S. Jiang[‡], N. Epperla, Y. Ma, M. Maadooliat, Z. Ye, B. Olson, M. Wang, T. Kitchner, J. Joyce, R. Stenn, J.J. Mazza, J.K. Meece, W. Wu, L. Jin, J.A. Smith, J. Wang, S.J. Schrodi (2019). A Gene-Based Recessive Diplotype Exome Scan Discovers FGF6, a Novel Hepcidin-Regulating Iron Metabolism Gene. Blood,133(88-98)

2. Epigenome architecture assembly to normal and disease tissues

Starting in 2015, I investigated the epigenetics of human disease with a particular focus on DNA methylation. I participated in several large projects to build a model of the epigenome architecture for human cells and tissues under normal and disease conditions. Notable work includes evaluating the genomic methylation profiles (methylomes) for normal human blood cells, animal model 'silk', CD4+ T-cells of patients with rheumatoid arthritis, pancreatic cancer cells, and hepatocellular carcinoma cells with different methylation methods, such as BS-seq and MBD-seq.

a. **Guo, S**[ǂ]., Q. Zhu[ǂ], T. Jiang, R. Wang, Y. Shen, X. Zhu, Y. Wang, F. Bai, Q. Ding, X. Zhou, G. Chen, and D.Y. He, Genome-wide DNA methylation patterns in CD4+ T cells from Chinese Han patients with rheumatoid arthritis. *Mod Rheumatol*, 2017. 27(3): p. 441-447. ([ǂ]Contributed equally)
b. Zhao, Y[ǂ]., F. Xue[ǂ], J. Sun[ǂ], **S. Guo**[ǂ], H. Zhang, B. Qiu, J. Geng, J. Gu, X. Zhou, W. Wang, Z. Zhang, N. Tang, Y. He, J. Yu, and Q. Xia, Genome-wide methylation profiling of the different stages of hepatitis B virus-related hepatocellular carcinoma development in plasma cell-free DNA reveals potential biomarkers for early detection and high-risk monitoring of hepatocellular carcinoma. *Clin Epigenetics*, 2014. 6(1): p. 30. ([ǂ]Contributed equally)
c. Zhao, Y[ǂ]., J. Sun[ǂ], H. Zhang[ǂ], **S. Guo**[ǂ], J. Gu, W. Wang, N. Tang, X. Zhou and J. Yu, High-frequency aberrantly methylated targets in pancreatic adenocarcinoma identified via global DNA methylation analysis using methylCap-seq. *Clin Epigenetics*, 2014. 6(1): p. 18. ([ǂ]Contributed equally)
d. Zhao, Y[ǂ]., **S. Guo**[ǂ], J. Sun[ǂ], Z. Huang, T. Zhu, H. Zhang, J. Gu, Y. He, W. Wang, K. Ma, J. Wang, and J. Yu, Methylcap-seq reveals novel DNA methylation markers for the diagnosis and recurrence prediction of bladder cancer in a Chinese population. *PloS one*, 2012. 7(4): p. e35175. ([ǂ]Contributed equally)

3. **Epigenetic variations and their use in diagnosing and treating complex diseases.**
   DNA methylation is known to be aberrant in the early stages of cancer. We identified a large number of methylation-based markers with diagnostic and prognostic implications for non-small cell lung cancer, bladder cancer, and pancreatic cancer. Since DNA methylation has different patterns for different tissue types, we proposed a prediction model to map the origin of cell-free DNA fragments based on tissue-specific methylation signals. This model provides a potential non-invasive approach for the diagnosis of solid cancers. In my current investigation, I am assessing the interaction effects of genetic variants with epigenetic variations in human complex diseases and applying these findings to the diagnosis and identification of disease subtypes.
   a. **Guo, S**., F. Yan, J. Xu, Y. Bao, J. Zhu, X. Wang, J. Wu, Y. Li, W. Pu, Y. Liu, Z. Jiang, Y. Ma, X. Chen, M. Xiong, L. Jin, and J. Wang, Identification and validation of the methylation biomarkers of non-small cell lung cancer (NSCLC). *Clin Epigenetics*, 2015. 7: p. 3.
   b. Geng, X., W. Pu, Y. Tan, Z. Lu, A. Wang, L. Tan, S. Chen, **S. Guo**[#], J. Wang[#], and X. Chen[#], Quantitative assessment of the diagnostic role of FHIT promoter methylation in non-small cell lung cancer. *Oncotarget*, 2017. 8(4): p. 6845-6856.
   c. Pu, W., C. Wang, S. Chen, D. Zhao, Y. Zhou, Y. Ma, Y. Wang, C. Li, Z. Huang, L. Jin, **S. Guo**[#], J. Wang[#], and M. Wang[#], Targeted bisulfite sequencing identified a panel of DNA methylation-based biomarkers for esophageal squamous cell carcinoma (ESCC). *Clin Epigenetics*, 2017. 9: p. 129.
   d. **Guo, S**[ǂ], D. Diep[ǂ], N. Plongthongkum, H.L. Fung, and K. Zhang, Identification of methylation haplotype blocks aids in deconvolution of heterogeneous tissue samples and tumor tissue-of-origin mapping from plasma DNA. *Nat Genet*, 2017. 49(4): p. 635-642. . ([ǂ]Contributed equally)

Complete List of Published Work:

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/45297273/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

CIBM: Phenome-wide association study maps genetic variation in epigenetic factors with human complex diseases.
Role: CIBM training grant for Dr. Guo

Genome-wide DNA methylation Patterns of Atrial Fibrillation Patients derived from Marshfield Clinic PMRP cohort
Role: Co-Investigator in collaboration with Dr. Ingrid Glurich and Dr. Michael Caldwell (PI)

Detecting shared chromosomal regions and compound heterozygous effects for diseases within PMRP
Role: Co-Investigator with Dr. Steven Schrodi

Sparse conditional generate adversarial networks for personalized biomarker selection and treatment effect estimation
Role: Co-Investigator with Dr. Momiao Xiong

Genome-wide DNA methylation profiling for a novel identified COL2A1 caused synovial chondromatosis pedigree
Role: Co-Investigator in collaboration with Dr. Steven Schrodi and Dr. Dongyi He

Genome-wide association study to identify novel susceptibility genes for rheumatoid arthritis
Role: Co-Investigator in collaboration with Dr. Steven Schrodi and Dr. Dongyi He

Genome-wide association study to identify novel pharmacogenomics genes for triple-therapy in rheumatoid arthritis
Role: Co-Investigator in collaboration with Dr. Steven Schrodi and Dr. Dongyi He

Completed Research Support

Unified Statistical Methods for Sequence-Based Association Studies. NIGMS

Role: Co-Investigator (2012-2015) in collaboration with Dr. Momiao Xiong (PI)

Statistical Methods for Finding Missing Heritability NHLBI
Role: Co-Investigator (2012-2014) in collaboration with Dr. Momiao Xiong (PI)

Understanding the genetic architecture of schizophrenia in Chinese population NIMH
Role: Co-Investigator (2013-2014) in collaboration with Dr. Momiao Xiong (PI)