Hongbo Liu

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EDUCATION & TRAINING

2018 - Now, Postdoctoral Fellow, Regulatory Genomics of Kidney Disease
Dr. Katalin Susztak's Lab, Institute for Diabetes, Obesity and Metabolism
Perelman School of Medicine, University of Pennsylvania

2016 - 2018, Postdoctoral Fellow, Epigenomics of Cancer
Dr. Hui Shen's Lab, Center for Epigenetics, Van Andel Institute

2012 - 2015, Ph.D., Biomedical Engineering (Developmental Biology and Epigenomics)
Dr. Qiong Wu's Lab, School of Life Science and Technology, Harbin Institute of Technology

2007 - 2010, MS, Biomedical Engineering (Bioinformatics and Epigenomics)
Dr. Yan Zhang's Lab, College of Bioinformatics Science and Technology, Harbin Medical University

2003 - 2007, BS, Information and Computing Science
School of Mathematical Sciences, Qufu Normal University

RESEARCH EXPERIENCE

The most significant research contributions during my postdoctoral and predoctoral training are focused on age-related chronic diseases (e.g., chronic kidney disease) as follows.

Genetic architecture and epigenetic regulation of chronic kidney disease (2018 - present)

- As an age-related chronic disease, kidney disease effect > 800 million people worldwide. To uncover the genetic basis of kidney disease, I performed the largest GWAS for kidney function (>1.5 million individuals) and discovered that epigenome (DNA methylation) explains a larger fraction of heritability than gene expression. To further identify disease-causal genes, I proposed a multi-stage prioritization strategy by integrating GWAS with various epigenomic datasets). Using this strategy, I prioritized >500 kidney disease genes, including *SLC47A1,* whose causal role was defined in mice with genetic loss of *Slc47a1* and in human individuals carrying loss-of-function variants. (*Liu et al., 2022 Nature Genetics* | *Project page* | *Github*).
- In my latest study, I expanded kidney function GWAS to 2.5 million individuals. To explore the regulatory potential of genetic variants, I investigated the allelic imbalance of chromatin state and gene expression driven by disease variants in individual and single-cell levels. Further, to prioritize disease-causal genes, I carried out single-cell multi-omic sequencing for open chromatin and gene expression in the same cell, and identified kidney disease cause genes driven by genetic variants. These results substantially improved the informativeness of disease mechanisms under age-related chronic diseases at GWAS loci (*Liu et al. In preparation*).
- To explore the contribution of epigenetic factors in age-related chronic diseases, I profiled DNA methylation by Whole-Genome Bisulfite Sequencing in mouse and human fetal kidneys and demonstrated essential functions of DNA methylation in decommissioned fetal enhancers linking to kidney disease (*Guan*, Liu* et al. 2020 JASN* | *Liu et al. In preparation*). Further, we performed epigenome-wide association studies (EWAS), and revealed the essential roles of DNA methylation in regulating kidney function and structure changes (*Sheng, Qiu, Liu, et al. 2020 PNAS* | *Yan*, Liu* et al. In preparation*). These studies highlighted locus-specific convergence of genetic, epigenetic, and developmental elements in the development of age-related chronic diseases.
- To identify cell types causally associated with kidney disease, we generated single-nucleus transposase-accessible chromatin with sequencing (snATAC-seq), single-cell RNA sequencing (scRNA), and spatially resolved transcriptomics in mouse and human kidneys. The analysis of these single-cell resolution datasets illustrated the crucial roles of kidney cells (e.g., proximal tubule cells) and cell type-specific genes (e.g., *SLC47A1*) in kidney injury and fibrosis. (*Liu et al., 2022 Nature Genetics* | *Sheng,…,Liu et al., 2021 Nature Genetics* | *Miao,…, Liu et*

al. 2021, Nature Comms | *Doke,…, Liu et al., 2021 JCI* | *Dhillion,…, Liu et al., Cell Metabolism* | *Amin,…, Liu et al. 2022 BioRxiv*). These studies highlighted the power of single-cell multi-omic data in uncovering cell origins of age-related chronic diseases.

Tissue-specific epigenetic regulation in development and age-related chronic diseases (2007 - 2017)

- To identify tissue-specific epigenetic regulatory elements, I developed a series of bioinformatic software, such as SMART for *de novo* identifying tissue/cell-specific methylated regions from whole genome bisulfite sequencing data (*Liu et al. 2016 NAR* | *Project page*); QDMR for identifying differentially methylated regions from array-based methylation data (*Zhang*, Liu* et al. 2011 NAR* | *Project page*); QDCMR for identifying differential chromatin regions from ChIP-seq data (*Liu et al. 2013 Scientific Reports* | *GitHub*).
- Leveraging these bioinformatic tools and large-scale epigenome data, I identified tissue-specific epigenetic regulatory elements, including DNA methylation, histone modifications, super-enhancers, and long non-coding RNAs, and explored their roles in mammalian development and age-related chronic diseases (*Liu et al. 2016 NAR* | *Liu et al. 2014 Database* | *Liu et al. 2013 Scientific Reports* | *Xu*, Liu* et al. 2019 Cell Death & Disease* | *Xiong,…, Liu✉ et al. 2017 NAR* | *Wei,…, Liu✉ et al. 2016 NAR* | *Lv*, Liu* et al. 2013 NAR* | *Lv*, Liu* et al. 2012 NAR* | *Zhang*, Liu* et al. 2011 NAR* | *Zhang*, Lv*, Liu* et al. 2010 NAR*).

SELECTED PEER-REVIEWED PUBLICATIONS

(Total citations: >1,700; H-index 24; *Contributed equally; ✉Corresponding author)

1. **Liu H**, Doke T, Guo D, Sheng X, Ma Z, Park J, Vy H, Nadkarni G, Abedini A, Miao Z, Palmer M, Voight B, Li H, Brown C, Ritchie M, Shu Y and Susztak K✉. (2022) Epigenomic and transcriptomic analyses define core cell types, genes and targetable mechanisms for kidney disease. ***Nature Genetics*****,** 54(7):950–962.
   Highlighted by: *Nature Genetics*, *Kidney International*
   Selected Media Reports: *GenomeWeb*, *Penn Medicine News*, *Penn Today*, *Mirage News*, *Medical Xpress*, *Technology Org*, *BioArt*, *ScienceNet*, *HealthTV*, *Read01*, *IndiaEducationDiary*
2. Guan Y*, **Liu H***, Ma Z, Li SY, Park J, Sheng X and Susztak K✉. (2020) Dnmt3a and Dnmt3b-Decommissioned Fetal Enhancers are Linked to Kidney Disease. ***Journal of the American Society of Nephrology***, 31(4), 765-782.
3. Xu S*, **Liu H***, Wan L*, Zhang W, Wang Q, Zhang S, Shang S, Zhang Y✉ and Pang D✉. (2019) The MS-lincRNA landscape reveals a novel lincRNA BCLIN25 that contributes to tumorigenesis by upregulating ERBB2 expression via epigenetic modification and RNA–RNA interactions in breast cancer. ***Cell Death & Disease***, 10(12), 920.
4. Xiong Y*****, Wei Y*****, Gu Y*****, Zhang S, Lyu J, Zhang B, Chen C, Zhu J, Wang Y, **Liu H**✉, Zhang Y✉ (2017) DiseaseMeth version 2.0: a major expansion and update of the human disease methylation database. ***Nucleic Acids Research***, 45(D1):D888-895.
5. **Liu H**✉*****, Liu X*****, Zhang S*****, Lv J, Li S, Shang S, Jia S, Wei Y, Wang F, Su J, Wu Q, and Zhang Y✉ (2016) Systematic identification and annotation of human methylation marks based on bisulfite sequencing methylomes reveals distinct roles of cell-type-specific hypomethylation in regulation of cell identify genes. ***Nucleic Acids Research***, 44(1):75-94.
6. Wei Y*****, Zhang S*****, Shang S*****, Zhang B, Wang X, Li S, **Liu H**✉, Zhang Y✉ (2016) SEA: a Super-Enhancer Archive. ***Nucleic Acids Research***, 44(D1):D172-179.
7. **Liu H*,** Zhu R*, Lv J*, He H, Yang L, Huang Z, Su J, Zhang Y, Yu S and Wu Q✉. (2014) DevMouse, the mouse developmental methylome database and analysis tools. ***Database***, 2014:bat084.
8. Lv J*, Huang Z*, Liu H*, **Liu H***, Cui W, Li B, He H, Guo J, Liu Q and Zhang Y and Wu Q✉. (2014) Identification and characterization of long intergenic non-coding RNAs related to mouse liver development. ***Molecular Genetics and Genomics***, 289(6), 1225-1235.
9. **Liu H***, Chen Y*****, Lv J*****, Zhu R, Su J, Liu X, Zhang Y✉, Wu Q✉ (2013) Quantitative epigenetic co-variation in CpG islands and co-regulation of developmental genes. ***Scientific Reports***, 3:2576.
10. Lv J*****, **Liu H***, Huang Z*****, Su J, He H, Xiu Y, Zhang Y and Wu Q✉ (2013) Long non-coding RNA identification over mouse brain development by integrative modeling of chromatin and genomic features. ***Nucleic Acids Research***, 41, 10044-10061.
11. Lv J*, Cui W*, **Liu H***, He H, Xiu Y, Guo J, Liu H, Liu Q, Zeng T, Chen Y and Wu Q✉. (2013) Identification and characterization of long non-coding RNAs related to mouse embryonic brain development from available transcriptomic data. ***PloS One***, 8, e71152.

12. Lv J*, **Liu H***, Su J*, Wu X, Li B, Xiao X, Wang F, Wu Q✉, Zhang Y✉ (2012) DiseaseMeth: a human disease methylation database. ***Nucleic Acids Research***, 40, D1030-1035.
13. Zhang Y✉*****, **Liu H***, Lv J*, Xiao X, Zhu J, Liu X, Su J, Li X, Wu Q, Wang F and Cui Y (2011) QDMR: a quantitative method for identification of differentially methylated regions by entropy. ***Nucleic Acids Research***, 39(9):e58.
14. Zhang Y✉*****, Lv J*****, **Liu H***, Zhu J, Su J, Wu Q, Qi Y, Wang F and Li X✉: (2010) HHMD: the human histone modification database. ***Nucleic Acids Research***, 38, D149-154.

Complete list of published work and citations in Google Scholar.

SOFTWARE & PLATFORMS

1. **Kidney_Epi_Pri**: Pipeline to perform multi-stage prioritization of disease causal genes by integrating GWAS with bulk and single-cell epigenome and transcriptome (*Liu et al. 2022 Nature Genetics*). Project page | Github
2. **SMART**: A Python package for deep analysis of DNA methylation by whole genome bisulfite sequencing, including genome segmentation based on DNA methylation and de novo identification of tissue/cell-specific methylated regions (*Liu et al. 2016 Nucleic Acids Research*). Project page | Github
3. **QDMR**: A Java Package for quantifying methylation difference and identifying differentially methylated regions across multiple conditions (*Zhang*, Liu* et al. 2011 Nucleic Acids Research*). Project page | Github
4. **QDCMR**: A Java package for quantifying chromatin modification difference and identifying DCMRs from genome-wide chromatin modification profiles (*Liu et al. 2013 Scientific Reports*). GitHub
5. **SEA**: A comprehensive online archive and analysis platform for super-enhancers in >200 cell types or tissues from 11 species (*Wei,…, Liu✉ et al. 2016 Nucleic Acids Research*). Project page
6. **DiseaseMeth**: A web-based resource and analysis platform for abnormal DNA methylation and related genes in >160 kinds of human diseases (Xiong*,…, Liu✉ et al. 2017 Nucleic Acids Research*). Project page

GRANTS

2015 - 2017 National Natural Science Foundation of China, #61403112 (PI: Hongbo Liu)

2012 - 2014 Foundation of Education Department of Heilongjiang Province, #12521270 (PI: Hongbo Liu)

2018 - 2022 National Institutes of Health NIH/NIDDK, #R01DK087635 (PI: Katalin Susztak)

2018 - 2022 National Institutes of Health NIH/NIDDK, #R01DK076077 (PI: Katalin Susztak)

2012 - 2014 National Natural Science Foundation of China, #31100948 (PI: Qianghu Wang)

2011 - 2013 National Natural Science Foundation of China, #61075023 (PI: Yan Zhang)

AWARDS

2022, Poster Prize in the Penn-Stanford CVI Symposium at the University of Pennsylvania

2019, Poster Prize in the Epigenetics Symposium at the Franklin Institute

2017, Science and Technology Award, Heilongjiang Province People's Government

2014, National Scholarship for Doctoral Students, Ministry of Education of China

2012, Science and Technology Award, Education Department of Heilongjiang Province

2011, Science and Technology Award, Science and Technology Department of Heilongjiang Province

2010, Outstanding Master's Degree Graduates, Heilongjiang Province Office of Education

TEACHING EXPERIENCE

Instructor: College of Bioinformatics Science and Technology, Harbin Medical University

Computational Epigenetics, Instructor, Fall 2015, Spring 2016

Biomolecular Network Analysis, Instructor, Spring 2011, Spring 2012, Spring 2016

Combinatorics and Graph Theory, Instructor, Fall 2015

Database Principles and Applications, Instructor, Fall 2011

System Biology, Instructor, Fall 2010

Advanced Mathematics, Instructor, Fall 2010

MENTORING EXPERIENCE

Instructor: College of Bioinformatics Science and Technology, Harbin Medical University

Shanshan Zhang (undergraduate), 2015 - 2016 (Now: Graduate student at Case Western Reserve University)

Shipeng Shang (undergraduate), 2014 - 2015 (Now: Assistant professor at Qingdao University)

Yunzhen Wei (undergraduate), 2013 - 2014 (Now: Assistant professor at Guangdong Medical University)

Rangfei Zhu (undergraduate), 2012 - 2014 (Now: CEO of Hangzhou Mugu Technology Co., Ltd)

COMPUTING SKILLS

R, Java, Python, C, HTML, Javascript, Linux shell, SQL.

SCIENTIFIC SOCIETIES

Editorial Board:

Briefings in Functional Genomics, 2016 - Present

Scientific Journal Reviewer:

Nucleic Acids Research, Human Molecular Genetics, Aging, Quantitative Biology, Molecular Therapy - Nucleic Acids, Genes, Briefings in Bioinformatics, Briefings in Functional Genomics, Frontiers in Genetics, Frontiers in Oncology, Frontiers in Cell and Developmental Biology, PLOS ONE, Oncotarget, Current Bioinformatics, Methods, The International Journal of Molecular Sciences.

Scientific Society Member:

The American Society of Human Genetics (ASHG); American Society of Nephrology (ASN); American Association for Cancer Research (AACR)

CONFERENCE & INVITED TALKS

10/07/2022 MidAtlantic Bioinformatics Conference (2022), Philadelphia, PA (Oral Presentation: *Kidney epigenome and transcriptome-based multi-stage prioritization defines core cell types, genes and targetable mechanisms for kidney disease*)

08/08/2022 International Conference on Intelligent Biology and Medicine (ICIBM), Philadelphia, PA (Oral Presentation: *Linking genetic variants to kidney disease via the epigenome*)

05/19/2022 Chinese Genomics Meet-up online, CGM online (Oral Presentation: *Epigenetic regulation and genetic variant annotation for kidney disease*)

04/25/2022 Penn Genetics 2022 Global Scientific Symposium, Philadelphia, PA (Oral Presentation: *Using single-cell multi-omics to translate human genetic hits*)

04/14/2022 Anhui Provincial Hospital, University of Science and Technology of China, Online (Oral Presentation: *The genetic basis and epigenetic regulation of complex disease*)

03/15/2022 Penn IDOM Spring Symposium, Philadelphia, PA (Poster Presentation: *Kidney epigenome and transcriptome-based multi-stage prioritization defines core cell types, genes and targetable mechanisms for kidney disease*)

12/16/2019 Fox Chase Cancer Center Epigenetics Symposium: 15 Years of Lysine Demethylases, Philadelphia, PA (Poster Presentation: *Dnmt3a and Dnmt3b-decommissioned fetal enhancers are linked to kidney disease*)

11/05/2019 Kidney Week 2019, American Society of Nephrology, Washington DC (Poster Presentation: *DNA Methylation Program in Human and Mouse Kidney Development*)

03/19/2019 Penn IDOM Spring Symposium, Philadelphia, PA (Poster Presentation: *DNA Methylation Program in Human and Mouse Kidney Development*)

03/06/2019 Keystone symposia: Unraveling the Secrets of Kidney Disease, Whistler Conference Centre, BC Canada (Oral Presentation: *Functional Methylome Analysis of Human Diabetic Kidney Disease*)

07/10/2016 The International Symposium on the Frontier of Big Data in Science, Baotou, China (Oral Presentation: *Cell Type-specific DNA Hypomethylation and Super Enhancer*)

12/17/2015 The 8th Guangzhou International Stem Cell and Regenerative Medicine Forum, Guangzhou, China (Poster Presentation: *An atlas of human methylation marks reveals hESC-specific hypomethylation at super-enhancers*)