Hong ZHENG, Ph.D.

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INTERESTS

Using computational biology and machine learning approaches to understand the **multi-omics landscape** (genomics, epigenomics, transcriptomics, *etc.*) and **immune responses** in human diseases (cancer, aging, infectious diseases, *etc.*), and identify **robust gene signatures and targets** for disease diagnostics, prognostics, and therapeutics.

PROFESSIONAL EXPERIENCE

2020-Present Stanford University

Research engineer and (previous) postdoctoral researcher in Khatri lab (khatrilab.stanford.edu). Current work focuses on **understanding immune responses** and **identifying gene signatures for diagnosis and prognosis** in **viral infections**, **aging**, and **cancer**.

- Pan-viral multi-cohort analysis of host immune response across viruses
 - Integrated transcriptome profiles of 4,780 blood samples from patients with one of 16 viral infections (influenza, SARS-CoV-2, Ebola, chikungunya, RSV, HRV, *etc.*) across 34 independent cohorts from 18 countries, and single-cell RNA-seq profiles of more than 264,000 immune cells from 71 samples across 3 independent cohorts.
 - Identified conserved protective and detrimental gene modules associated with severity, regardless of the infecting virus.
 - The largest and most comprehensive systems immunology analysis of host immune response to viral infection to date.
 - Presented opportunities for the development of diagnostics, prognostics, and host-directed antiviral therapies for a broad spectrum of viruses that could facilitate risk stratification and targeted treatment of patients and improve global pandemic preparedness.
- Work in progress
 - Multi-cohort meta-analysis of immune responses in infectious diseases from single-cell RNA-Seq profiling.
 - Identifying gene signatures from blood transcriptome for early diagnosis of neurodegenerative diseases and lung cancer.

2017-2020 Stanford University

Postdoctoral researcher in Gevaert lab (med.stanford.edu/gevaertlab.html). Worked on transcriptome analysis and machine learning applications in biomedical research.

- **Benchmarking RNA sequencing analysis pipeline.** Evaluated several key aspects in RNA sequencing analysis, including nine common workflows, protocols for library preparation (un-stranded vs. strand-specific), and transcriptome annotation, which provided timely and useful recommendations for the research community.
- Long noncoding RNAs in cancer. Re-analyzed RNA-seq data from over 10k samples in TCGA and provided more updated and accurate gene expression profiles.
 - Machine learning applications in biomedical research
 - **Integration of imaging and molecular data**. Applied machine learning methods to link DNA methylation patterns to imaging features in cancer samples.
 - **Missing data imputation**. Helped in evaluating the methods for imputing missing values in genomic data, including KNN, SVD, and variational auto-encoder (VAE).
 - **Meta-learning for genomic survival analysis in cancer**. Helped in developing a meta-learning framework based on neural networks for survival analysis in cancer through leveraging high-dimensional genomic data.

2012-2016 The University of Hong Kong

Ph.D. candidate in the lab of Prof. Maria Li Lung, Department of Clinical Oncology, Faculty of Medicine, studying the genetic and genomic basis of nasopharyngeal carcinoma (NPC), a unique Epstein-Barr virus (EBV)-associated subtype of head and neck cancer. My research has greatly advanced understanding of the molecular changes and genetic predisposition of NPC, which provides new perspectives for the rational development of diagnostics, prognostics, and targeted therapies.

Ph.D thesis: Identification of genetic susceptibility genes and characterization of somatic mutations in nasopharyngeal carcinoma (available at *hub.hku.hk/handle/10722/270220*)

- Somatic mutation landscape study. Paired tumor and blood samples were sequenced using WES and RNA-Seq to characterize the mutation landscape and signatures in NPC tumors and to identify significantly mutated genes and pathways. The most significant finding is multiple loss-of-function mutations in several NF- \varkappa B signaling negative regulators. The study improved the understanding of the molecular changes in NPC and highlighted the critical role of NF- \varkappa B signaling in NPC.
- Genetic susceptibility study. WES and targeted sequencing were used to examine blood samples of cancer cases and controls to identify genes or pathways associated with disease risk. Pathogenic germline variants in macrophage stimulating 1 receptor (*MST1R*) gene were enriched in early-age-onset NPC cases. This gene plays important roles in host defense and immune response. This is the first study to fully characterize the germline variants in NPC patients using DNA sequencing approach and highlights the importance of MST1R signaling in the pathogenesis of NPC.

2010-2012 Peking University, Beijing, China

Worked at the State Key Laboratory of Protein and Plant Gene Research, studying plant pathogens and host defense responses, particularly the role of small RNAs and host microRNAs in the defense response of *Oryza sativa* against two rice viruses. Conducted both benchtop experiments and data analysis from Solexa/Illumina high throughput sequencing data.

EDUCATION

Ph.D.	2012-2016	Clinical Oncology/Cancer Genomics
		The University of Hong Kong, Hong Kong, China
B.E.	2006-2010	Biomedical Engineering, Xi'an Jiaotong University, China
		Graduated with Distinguished Graduate Student Award

SKILLS

- Extensive hands-on experiences in **bioinformatics toolkits and pipelines**. Familiar with **cloud computing platforms** (AWS and GCP), **Docker**, and building web apps using **Shiny**.
- Experienced in **meta-analysis** and **large-scale sequencing datasets**, including the Cancer Genome Atlas (TCGA), The Genotype-Tissue Expression (GTEx), and NCBI SRA/GEO.
- Intensive analysis and interpretation skills of next-generation sequencing/multi-omics datasets:
 - Genetics and genomics
 Whole exome sequencing | whole genome sequencing | Germline and somatic variant calling and interpretation | GWAS
 - Transcriptomics
 Bulk cell RNA-Seq | Single-cell RNA-Seq | Trajectory analysis | Variant calling | HLA typing | Pathogen detection
 - Epigenetics and epigenomics ATAC-seq | single-cell ATAC-seq | HumanMethylation450 array | Bisulfite sequencing | ChIP-Seq
 - **Proteomics** CyTOF | Olink | Luminex
- Familiar with statistical methods, high-dimensional data analysis, and machine learning algorithms.
- Profound knowledge in **cancer genomics** and **immunology**.
- Excellent data visualization skills
 - Poster made with R only: <u>https://f1000research.com/posters/9-1410</u>
- Programming languages R | Bash | Python | Perl | MATLAB | SQL | C++
- Experimental skills DNA/RNA extraction | PCR and quantitative PCR
- Languages English | Chinese | Cantonese | German | Russian

PUBLICATIONS

 Chen G, Deutsch GH, Schulert GS, Zheng H, Jang S, Trapnell B, et al. Identification of Distinct Inflammatory Programs and Biomarkers in Systemic Juvenile Idiopathic Arthritis and Related Lung Disease by Serum Proteome Analysis. Arthritis Rheumatol. 2022;74(7):1271–83

- 2. Brennan K, **Zheng H**, Fahrner JA, Shin JH, Gentles AJ, Schaefer B, et al. NSD1 mutations deregulate transcription and DNA methylation of bivalent developmental genes in Sotos syndrome. *Hum Mol Genet.* 2022 Jan 31
- 3. Buturovic L^{*}, **Zheng H**^{*}, Tang B, Lai K, Kuan WS, Gillett M, et al. A 6-mRNA host response classifier in whole blood predicts outcomes in COVID-19 and other acute viral infections. *Sci Rep.* 2022 Jan 18;12(1):889. *contributed equally
- 4. Xie P*, **Zheng H***, Chen H, Wei K, Pan X, Xu Q, et al. Tumor response as defined by iRECIST in gastrointestinal malignancies treated with PD-1 and PD-L1 inhibitors and correlation with survival. *BMC Cancer.* 2021 Nov 19;21(1):1246. *contributed equally
- 5. **Zheng H**^{*}, Rao AM^{*}, Dermadi D^{*}, Toh J^{*}, Jones LM^{*}, Donato M^{*}, et al. Multicohort analysis of host immune response identifies conserved protective and detrimental modules associated with severity across viruses. *Immunity*. 2021 Apr 13;54(4):753-768.e5. *contributed equally
- 6. Qiu YL, **Zheng H**, Devos A, Selby H, Gevaert O. A meta-learning approach for genomic survival analysis. *Nat Commun.* 2020 Dec 11;11(1):6350.
- 7. Qiu YL, **Zheng H**, Gevaert O. Genomic data imputation with variational autoencoders. *GigaScience*. 2020 Aug 1;9(8).
- 8. **Zheng H**, Momeni A, Cedoz P-L, Vogel H, Gevaert O. Whole slide images reflect DNA methylation patterns of human tumors. *NPJ Genomic Med.* 2020;5:11.
- 9. **Zheng H**, Brennan K, Hernaez M, Gevaert O. Benchmark of long non-coding RNA quantification for RNA sequencing of cancer samples. *GigaScience*. 2019 01;8(12).
- 10. Lin W, Yip YL, Jia L, Deng W, **Zheng H**, Dai W, *et al.* Establishment and characterization of new tumor xenografts and cancer cell lines from EBV-positive nasopharyngeal carcinoma. *Nat Commun.* 2018 Nov 7;9(1):4663.
- Bakr S, Gevaert O, Echegaray S, Ayers K, Zhou M, Shafiq M, Zheng H, et al. A radiogenomic dataset of non-small cell lung cancer. Sci Data. 2018 Oct 16;5(1):1–9.
- 12. Dai W, Ko JMY, Choi SSA, Yu Z, Ning L, Zheng H, et al. Whole-exome sequencing reveals critical genes underlying metastasis in oesophageal squamous cell carcinoma. J Pathol. 2017 Aug;242(4):500–10.
- 13. Zheng H*, Dai W*, Cheung AKL*, Ko JMY, Kan R, Wong BWY, et al. Wholeexome sequencing identifies multiple loss-of-function mutations of NF-*κ*B pathway regulators in nasopharyngeal carcinoma. Proc Natl Acad Sci U S A. 2016 Oct 4;113(40):11283–8. *contributed equally
- Dai W*, Zheng H*, Cheung AKL, Tang CS, Ko JMY, Wong BWY, et al. Wholeexome sequencing identifies MST1R as a genetic susceptibility gene in nasopharyngeal carcinoma. Proc Natl Acad Sci U S A. 2016 Mar 22;113(12):3317– 22. *contributed equally
- 15. Dai W[,] Zheng H, Cheung AKL, Lung ML. Genetic and epigenetic landscape of nasopharyngeal carcinoma. *Chin Clin Oncol.* 2016 Apr;5(2):16.
- 16. Dai W, Cheung AKL, Ko JMY, Cheng Y, **Zheng H**, Ngan RKC, *et al.* Comparative methylome analysis in solid tumors reveals aberrant methylation at chromosome 6p in nasopharyngeal carcinoma. *Cancer Med.* 2015 Jul;4(7):1079–90.
- 17. Wu J, Yang Z, Wang Y, Zheng L, Ye R, Ji Y, Zhao S, Ji S, Liu R, Xu L, **Zheng H**, *et al.* Viral-inducible Argonaute18 confers broad-spectrum virus resistance in rice by sequestering a host microRNA. *eLife.* 2015 Feb 17;4.
- Jiang L, Qian D, Zheng H, Meng L-Y, Chen J, Le W-J, et al. RNA-dependent RNA polymerase 6 of rice (Oryza sativa) plays role in host defense against negative-strand RNA virus, Rice stripe virus. Virus Res. 2012 Feb;163(2):512–9.

19. Du P, Wu J, Zhang J, Zhao S, **Zheng H**, Gao G, *et al.* Viral infection induces expression of novel phased microRNAs from conserved cellular microRNA precursors. *PLoS Pathog.* 2011 Aug;7(8):e1002176.

PRESENTATIONS AND CONFERENCES

2022 Poster presentation at ASM Microbe, Washington DC, June 9-13, Identification of Conserved Detrimental Host Immune Response Predicts Severity of Bacterial and Viral Infections

2021 Oral presentation at Stanford Immunology Scientific Conference, Pacific Grove, Nov. 12-13. Multi-cohort analysis of host immune response identifies conserved protective and detrimental modules associated with severity across viruses

2021 Poster presentation at Pacific Symposium on Biocomputing (PSB), Jan. 5-7, Multicohort analysis of host immune response identifies conserved protective and detrimental modules associated with severity irrespective of virus

2018 Poster presentation at AACR Annual Meeting, Chicago, April 14-18, Benchmark of lncRNA Quantification for RNA-Seq of Cancer Samples

2016 Invited talk, Nasopharyngeal Carcinoma Gordon Research Conference, Hong Kong, June 26 - July 1, Identification of genetic susceptibility genes in nasopharyngeal carcinoma by next-generation sequencing

2016 Poster presentation at AACR Annual Meeting, New Orleans, April 16-20, Wholeexome sequencing identifies NF-xB pathway regulators frequently mutated in nasopharyngeal carcinoma

2015 Poster presentation at AACR Annual Meeting, Philadelphia, April 18-22, Unraveling the genetic basis of nasopharyngeal carcinoma using next-generation sequencing approaches

PROFESSIONAL MEMBERSHIPS

2014-present Associate member of American Association for Cancer Research (AACR)

AWARDS AND HONORS

2017	Summer Institutes Scholarship, Department of Biostatistics, University of
	Washington
2016	Y S and Christabel Lung Postgraduate Scholarship, The University of
	Hong Kong
2012-2016	Postgraduate Scholarship, The University of Hong Kong
2011	Excellent Academic Performance Scholarship, Peking University
2011	Dupont Scholarship, Peking University
2007-2010	Cyrus Tang Scholarship
2010	Distinguished Graduate Student Award, Xi'an Jiaotong University
2007-2009	Distinguished Student Xi'an Jiaotong University
2008-2010	Siyuan Scholarship, Xi'an Jiaotong University

TEACHING AND MENTORING

2019 Mentor, Stanford Canary CREST Program; Mentee: Megan Li; Project: Gene Regulatory Module Network Analysis of Cancer from Bulk and Single-cell RNA Sequencing

- 2018 Mentor, Stanford Canary CREST Program; Mentee: Irmina Benson; Project: Learning bioinformatics and Differential Gene Expression Analysis of RNA-Seq data
- 2018 Instructor, Principles of Cancer Systems Biology (CBIO 243), DNA methylation analysis, Stanford University
- 2011 Teaching assistant, New Thinkings of Life Science, School of Life Sciences, Peking University
- 2011 Teaching assistant, Molecular Virology, School of Life Sciences, Peking University

NON-ACADEMIC WORK

Consulting

2016-2017

Bioinformatics consultant, Prenetics Limited, Hong Kong, China

Developed next-generation sequencing analysis pipeline for detection and annotation of disease-related genetic alterations. My work aided in the development of the company's hereditary cancer panel product.

Science communication

- 2020-present Science writer on cancer, communicating latest advances in cancer research and treatment to cancer patients
- 2010-2019 Science writer of guokr.com and Caixin Global