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: Fei Chen

eRA COMMONS USER NAME (credential, e.g., agency login): MEGAN18988

POSITION TITLE: Assistant 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
Fudan University, Shanghai, China	B.S.	07/2007	Biological Sciences
Columbia University, New York, NY	M.A.	05/2010	Biomedical Informatics
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD	Sc.M.	05/2014	Epidemiology
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD	Ph.D.	12/2018	Epidemiology
University of Southern California, Los Angeles, CA	Postdoctoral	09/2022	Genetic Epidemiology

A. Personal Statement

Trained as a genetic epidemiologist, my primary research focuses on understanding the genetic contribution to the risk and racial disparities of common cancer. I have completed several large-scale genome-wide association studies (GWAS), whole-exome sequencing (WES), and whole-genome sequencing (WGS) analyses examining the effect of single nucleotide variants (SNVs) in the susceptibility of pancreatic, prostate, and breast cancer across ancestry populations. As an investigator of the Multiethnic Cohort (MEC) Study, a large prospective cancer cohort of over 215,000 White, African American, Latino, Japanese American, and Native Hawaiian men and women, I have expanded my work into investigating non-genetic factors and gene-environment (GxE) interactions for prostate and breast cancer, and the genetic susceptibility of second primary cancer (SPC) in breast cancer survivors. My research thus far had led to 17 publications (9 first-author publications), with many in prominent journals such as *JAMA Oncology*, *European Urology*, *Cancer Research*, and *American Journal of Respiratory and Critical Care Medicine*, as well as 8 conference posters and 5 oral presentations.

In this proposed research, I will contribute my expertise and experience in analyzing large-scale genotyping and sequencing data in family-based studies. Recently, I collaborated with colleagues at the Center for Inherited Disease Research (CIDR) and USC Center for Genetic Epidemiology in establishing pipelines for detecting copy number variations (CNVs) using genotyping and/or WES data in admixed populations. These pipelines will provide critical support to understanding the contribution of CNVs to the familial risk of prostate cancer.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2013 - 2014	Research Assistant, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
2014 - 2018	Research Assistant, Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD

2019 - 2022	Postdoctoral Scholar, Department of Population and Public Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA
2022 -	Assistant Professor, Department of Population and Public Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA

Other Experience and Professional Memberships

2014 -	Member, International Genetic Epidemiology Society
2014 -	Member, American Society of Human Genetics
2020 -	Associate, American Association for Cancer Research (AACR)

Honors

2013 - 2014	Master's Tuition Scholarship, Johns Hopkins Bloomberg School of Public Health
2014 - 2018	Fellowship, The Maryland Genetics, Epidemiology, and Medicine Training Grant
2015 - 2016	The Wolfe Street Competition Award, Johns Hopkins Bloomberg School of Public Health

C. Contributions to Science

1. As a doctoral student and a pre-doctoral trainee of the Maryland Genetics, Epidemiology and Medicine (MD-GEM) Fellowship Program at Johns Hopkins Bloomberg School of Public Health, my research initially focused on the effects of rare and low-frequency SNVs on the etiology of complex traits and diseases. In the Beaver Dam Eye Study, I conducted two rare variant association analyses that linked several genes to elevated intraocular pressure and refractive errors, which are two risk factors for open-angle glaucoma, a major cause of blindness for people over the age of 60. Using WES data, I performed the first linkage study in families with pulmonary nontuberculous mycobacterial disease (PNTM) which mapped a 20-cM linkage region on chromosome 6q12-6q16 and identified *TTK* (TTK protein kinase gene) as the candidate gene for PNTM within the region. Motivated by the rising burden of cancer in the United States and globally, I later shifted my research focus to the genetic etiology of cancer. Applying the analytical skills from my research in non-cancer phenotypes, I conducted a heritability analysis using both imputed genotyping data and WGS data to decipher the genetic architecture of pancreatic cancer. This analysis highlights the disproportionate contribution of rare and coding SNVs to the susceptibility of pancreatic cancer, which emphasizes the importance of large sequencing studies where the impact of rare variants can be adequately assessed on a genome-wide scale.

    a. **Chen F**, Klein AP, Klein BE, Lee KE, Truitt B, Klein R, Iyengar SK, Duggal P. Exome array analysis identifies CAV1/CAV2 as a susceptibility locus for intraocular pressure. Investigative ophthalmology & visual science. 2015 Jan 1;56(1):544-51.
    b. **Chen F**, Duggal P, Klein BE, Lee KE, Truitt B, Klein R, Iyengar SK, Klein AP. Variation in PTCHD2, CRISP3, NAP1L4, FSCB, and AP3B2 associated with spherical equivalent. Molecular vision. 2016;22:783.
    c. **Chen F**, Szymanski EP, Olivier KN, Liu X, Tettelin H, Holland SM, Duggal P. Whole-exome sequencing identifies the 6q12-q16 linkage region and a candidate gene, TTK, for pulmonary nontuberculous mycobacterial disease. American journal of respiratory and critical care medicine. 2017 Dec 15;196(12):1599-604.
    d. **Chen F**, Childs EJ, Mocci E, Bracci PM, Gallinger S, Li D, Neale RE, Olson SH, Scelo G, Bamlet WR, Blackford AL. Analysis of heritability and genetic architecture of Pancreatic Cancer: A PanC4 Study. Cancer Epidemiology and Prevention Biomarkers. 2019 Jan 1:cebp-1235.

2. Prostate cancer is the second leading cause of cancer death and represents one of the largest health disparities in the United States, with African ancestry men having the highest incidence rates. As a postdoctoral scholar and recipient of the T32 Multidisciplinary Training Fellowship in Ethnic Diversity and Cancer Disparities at the USC Keck School of Medicine, an important part of my research focuses on the contribution of genetic factors to the susceptibility of prostate cancer in diverse populations. Using genetic data from the VA Million Veteran Program (MVP), UK Biobank, and several smaller studies, I validate a previously developed multi-ancestry polygenic risk score

(PRS) as an effective prostate cancer risk stratification tool in European, African, and Hispanic populations. I have recently completed the largest genetic analysis of prostate cancer to date in men of African ancestry combining GWAS summary statistics in 19,378 cases and 61,620 controls from ten consortia and biobanks (Manuscript in review). This analysis led to the discovery of nine novel prostate cancer risk variants, of which seven were only found or substantially more common in men of African ancestry, which underscores the importance of large-scale genetic analysis in men of African ancestry for understanding prostate cancer susceptibility and disease biology in this high-risk population. More importantly, this study provided the first evidence that a multi-ancestry PRS could distinguish aggressive and non-aggressive prostate cancer in African ancestry men. In addition to common genetic variants, rare pathogenic variants (PVs) are known to contribute to the susceptibility of prostate cancer. I am currently carrying out a large WES analysis using data from the Research on Prostate Cancer in Men of African Ancestry: Defining the Roles of Genetics, Immunity and Stress (RESPOND) Consortium, investigating the association of rare PVs and variants of uncertain significance (VUS) with risk of overall prostate cancer and aggressive prostate cancer in 7,176 prostate cancer cases and 4,8723 controls of African ancestry.

a. **Fei Chen**[*], Burcu F Darst[*], Ravi K Madduri, Alex A Rodriguez, Xin Sheng, et al. (2022) Validation of a multi-ancestry polygenic risk score and age-specific risks of prostate cancer: a meta-analysis within diverse populations eLife 11:e78304. *[*]Shared first authorship*
b. **Chen F**, Madduri RK, Rodriguez A, … Haiman CA. Evidence of novel susceptibility variants for prostate cancer and a polygenic risk score associated with aggressive disease in men of African ancestry (*in review*).

3. The lack of modifiable risk factors for prostate cancer has motivated me to explore the influence of non-genetic factors and gene-environment (GxE) interactions on risk of prostate cancer. Using the epidemiologic data from the Multiethnic Cohort Study (MEC), I assessed the chemo-preventive effect of pre-diagnostic statin use on prostate cancer incidence and mortality across Whites, African Americans, Japanese Americans, Native Hawaiians, and Latinos. Findings from this study support the potential benefits of statins in reducing the risk and mortality of prostate cancer, especially aggressive disease. The etiology of cancer is multi-factorial, likely involving a complex interaction of genetic and non-genetic factors. Studying GxE interactions can provide valuable insights into the biology of disease and characterize the genetic subgroups with higher exposure-specific disease risk where public health preventive interventions may be more effective. To explore my interest in GxE interactions and cancer risk, I developed a research proposal to investigate the interactions between PRS and body mass index (BMI), physical activity, and dietary patterns on risk of prostate, breast, and colorectal cancer in MEC. This project is now supported by an Investigator-Initiated Research Grant from the American Institute of Cancer Research (AICR).

a. **Chen F**, Wan P, Wilkens LR, Le Marchand L, Haiman CA (2022). The association of prediagnostic statin use with aggressive prostate cancer from the Multiethnic Cohort Study. Cancer Epidemiol Biomarkers Prev.
b. Alisha Chou, **Fei Chen**, Peggy Wan, Xin Sheng, Song-Yi Park, Daniel O. Stram, Lynne R. Wilkens, Loïc Le Marchand, Christopher A. Haiman. Interactions of a polygenic risk score and modifiable lifestyle factors for breast cancer in the Multiethnic Cohort Study [Abstract]. AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved. September 16-19, 2022; Philadelphia, Pennsylvania.

4. Breast cancer is the most common cancer and the second leading cause of cancer death among women in the United States. African American women are more likely to be diagnosed with breast cancer before age 50 and had the highest mortality rate than any other racial/ethnic group. To evaluate whether genetics contribute to racial disparities and if the self-reported race should inform strategies for genetic testing, I collaborated with investigators from the Cancer Risk Estimates Related to Susceptibility (CARRIERS) consortium in a study where we found the prevalence of PVs in breast cancer susceptibility genes was similar between African American and White women. These findings suggest that equal access and update of genetic testing should be independent of self-reported race/ethnicity. Women who have had breast cancer in the past are at increased risk of developing a second primary cancer (SPC). Identifying risk factors for SPC is essential for cancer prevention efforts, especially with an increasing population of breast cancer survivors. In a multiethnic cohort analysis of 3,223 female MEC breast cancer patients with sequencing data from the CARRIERS consortium, I evaluated the PVs in 37 cancer predisposition genes for association with SPC. Findings from

this study linked germline PVs in *BRCA1*, *BRCA2*, and *ERCC2* to the development of SPC, and suggest that compromised DNA repair mechanisms could be a predisposition factor for SPC in breast cancer patients.

a. Domchek SM*, Yao S*, **Chen F***, et al. Comparison of the Prevalence of Pathogenic Variants in Cancer Susceptibility Genes in Black Women and Non-Hispanic White Women with Breast Cancer in the United States. JAMA Oncol. 2021;7(7):1045-1050. doi:10.1001/jamaoncol.2021.1492. **Shared first authorship*

b. **Chen F**, Park SL, Wilkens LR, Wan P, Hart SN, Hu C, Yadav S, Couch FJ, Conti DV, de Smith AJ, Haiman CA. Genetic Risk of Second Primary Cancer in Breast Cancer Survivors: The Multiethnic Cohort Study. Cancer Res. 2022 Sep 16;82(18):3201-3208. doi: 10.1158/0008-5472.CAN-21-4461. PMID: 35834270; PMCID: PMC9481694.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/fei.chen.3/bibliography/public/