BIOGRAPHICAL SKETCH

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NAME: Chiang, Charleston

eRA COMMONS USER NAME (credential, e.g., agency login): CCHIANG2

POSITION TITLE: Assistant Professor of Population and Public Health Sciences

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
UCLA, Los Angeles, CA	BS	06/2005	Microbiology, Immunology, and Molecular Genetics
Harvard University, Cambridge, MA	PHD	03/2011	Genetics
UCLA, Los Angeles, CA	Postdoc	03/2015	Population Genetics
UCLA, Los Angeles, CA	Postdoc	11/2017	Human Genetics

A. Personal Statement

I am an Assistant Professor at the University of Southern California (USC), affiliated with the Center for Genetic Epidemiology in the Department of Population and Public Health Sciences at USC's Keck School of Medicine as well as with the Department of Quantitative and Computational Biology at USC's Dornsife College of Arts and Sciences. I am a human geneticist, with a strong interest in using genomic data to understand how differences in complex trait architecture arise between diverse populations due to population genetic forces such as demographic history or natural selection. These insights will be critical for understanding health disparity between populations, for practicing and realizing personalized medicine, and for designing more powerful and inclusive genomic studies. I have led past and ongoing genome-wide association studies (GWAS) to map genetic loci underlying human complex traits in diverse populations, including cohorts of African Americans, Sardinians, and Finns. I have extensively investigated the evolutionary forces that shaped the pattern of genetic and phenotypic variation. This work consists of devising methods and investigating population structure and demographic history of populations from Sardinia, Finland, and China, and the inference of polygenic adaptation of human complex traits. My current research program brings these different aspects of medical and population genetics together to understand the evolution of complex traits within and between diverse, often underserved, populations, such as the indigenous population of Native Hawaiians and ethnic minority Latino populations. In addition, I am actively developing statistical genetic methods that would incorporate principles of evolutionary and population genetics to enhance the design, analysis, and interpretation of human genetic studies.

Current Research Support:
R35GM142783 Chiang (PI) 08/01/2021-07/31/2026
An evolutionary framework to elucidate and interpret the genetic architecture of complex traits in diverse populations

R01HG011646 Chiang (PI) 09/01/2022-08/31/2027
Leveraging the evolutionary history to improve identification of trait-associated alleles and risk stratification models in Native Hawaiians

Citations:

a. **Chiang CWK**†, Marcus J, Sidore C, Biddanda, A, Al-asadi H, Zoledziewska M, Pitzalis M, Busonero F, Maschio A, Pistis G, Steri M, Angius A, Lohmueller KE, Abecasis G, Schlessinger D, Cucca F, Novembre J†. "Genomic history of the Sardinian population." **Nat Genet.** 2018 Oct;50(10):1426-1434. doi 10.1038/s41588-018-0215-8 **(† corresponding author)**
b. Locke AE*, Steinberg KM*, **Chiang CWK***, Service S*, Havulinna A, Stell L, Pirinen M, Abel HJ, Chiang CC, Fulton RS, Jackson AU, Kang CJ, Kanchi KL, Koboldt DC, Larson DE, Nelson J, Nicholas TJ, Pietila A, Ramensky V, Ray D, Scott LJ, Stringham HM, Vangipurapu J, Welch R, Yajnik P, Yin X, Eriksson JG, Ala-Korpela M, Jarvelin MR, Manniko M, Laivouri H, FinnGen Project, Dutcher SK, Stitziel NO, Wilson RK, Hall IM, Sabatti C, Palotie A, Salomaa V, Laakso M, Ripatti S, Boehnke M, Freimer NB. "Exome sequencing of Finnish isolates enhances rare-variant association power." **Nature.** 2019 Aug;572(7769):323-328. doi: 10.1038/s41586-019-1457-z **(* joint first author)**
c. Chen M, Sidore C, Akiyama M, Ishigaki K, Kamatani Y, Schlessinger D, Cucca F, Okada Y, **Chiang CWK**. "Evidence of polygenic adaptation in Sardinia at height-associated loci ascertained from the Biobank Japan." **Am J Hum Genet**. 2020 Jul 2;107(1):60-71. doi: 10.1016/j.ajhg.2020.05.014.
d. Fan C†, Mancuso N*, **Chiang CWK***†. "A genealogical estimate of genetic relationships" **Am J Hum Genet** 2022 May 4; 109(5):812-824. doi: 10.1016/j.ajhg.2022.03.016 **(* joint senior author, † joint corresponding author)**

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 - present	Assistant Professor, University of Southern California, Department of Biological Sciences, Quantitative Computational Biology Section, Los Angeles, CA
2017 - present	Assistant Professor, University of Southern California, Keck School of Medicine, Department of Preventive Medicine, Center for Genetic Epidemiology, Los Angeles, CA
2015 - 2017	Postdoctoral Fellow, UCLA, Semel Institute for Neuroscience and Human Behavior, Center for Neurobehavioral Genetics, Los Angeles, CA
2011 - 2015	Postdoctoral Fellow, UCLA, Department of Ecology and Evolutionary Biology, Los Angeles, CA

Other Professional Positions and Appointments

2021-2023	Member, Awards Committee, American Society of Human Genetics (ASHG)
2021	Ad hoc external grant reviewer, NSF CAREER program
2020 - present	Member, American Association of Physical Anthropologists
2019	Mentor, Trainee-Mentor Luncheon, ASHG 2019, Evolution and Population Genetics
2019	Ad hoc external grant reviewer, Medical Research Council NIRG
2018	Ad hoc external grant reviewer, Human Frontier Science Program
2018	Symposium organizer, 1st AsiaEvo Conference at Shenzhen, China
2014 - present	Member, Society of Molecular Biology and Evolution (SMBE)
2011 - present	Ad hoc reviewer for over 19 journals, including: *Nature, Science, Nature Genetics, American Journal of Human Genetics, PLoS Genetics, Nature Communication, Science Advances, Molecular Biology and Evolution*
2007 - present	Member, American Society of Human Genetics (ASHG)

Honors

2017	Charles J. Epstein Trainee Award for Excellence in Human Genetics Research (semifinalist), American Society of Human Genetics
2013 - 2015	NIH NRSA Postdoctoral Fellowship, National Institute of Health, NIGMS

2010	Summer Institute in Statistical Genetics Travel Scholarship, University of Washington
2007 - 2010	NSF Graduate Fellowship, National Science Foundation
2005	Director's Fellowship (declined), Yale University
2005	Phi Beta Kappa Society, UCLA
2004	Ira J. and Shirley Spoon Honors Collegium Scholarship, UCLA
2003	Golden Key International Honour Society, UCLA
2001	Phi Eta Sigma Honor Society, UCLA
2001	CRC Press Freshmen Chemistry Achievement Award, UCLA
2001	Alpha Lambda Delta Honor Society, UCLA
2001	The National Society of Collegiate Scholars, UCLA

C. Contributions to Science

1. Understanding the genetic architecture of diverse populations. Human genetic studies have thus far focused on aggregating ever increasing number of individuals of Western European ancestry, resulting in disparity in applying genetics to medicine. There is an increasing recognition of this problem, but the scale of studying diverse populations lags significantly behind that of studies of Europeans. Ever since the dawn of genome-wide association studies, I have focused on and led genetic studies in mapping genetic loci underlying human complex phenotypes in non-European populations, such as African Americans and Latino Americans. I have also studied European populations with special demographic histories, such as the Sardinians and Finns, in order to develop a framework that leverages population history to improve the design and interpretation of genetic association studies. This framework will be particularly valuable when applied to diverse ethnic minority populations, which tend to have a unique evolutionary path that contributed to the disparity they experience today. My major accomplishments include (1) conducting one of the first genome-wide association studies of anthropometric traits in African Americans and Jamaicans and investigating its genetic architecture in comparison to those of the European-ancestry populations; (2) identifying alleles at known Mendelian genes that influence the distribution of height at the population level, and that pleiotropy and parent-of-origin effects can significantly impact the complex trait architecture; (3) leveraging special demographic history to empower successful identification of novel and rare variants associated with cardiometabolic traits; and (4) extending genome-wide association studies to diverse multiethnic populations for rare diseases such as acute lymphoblastic leukemia.

1a. Kang SJ*, **Chiang CWK***, Palmer CD*, Tayo BO, Lettre G, Butler JL, Hackett R, Adeyemo AA, Guiducci C, Berzins I, Nguyen TT, Feng T, Luke A, Shriner D, Ardlie K, Rotimi C, Wilks R, Forrester T, McKenzie CA, Lyon HN, Cooper RS, Zhu X, Hirschhorn JN. “Genome wide association of anthropometric traits in African and African derived populations.” **Hum Mol Genet.** 2010 Jul 1;19(13):2725-38. doi: 10.1093/hmg/ddq154. **(* joint first author)**

1b. Zoledziewska M*, Sidore C*, **Chiang CWK***, Sanna S*, Mulas A, Steri M, Busonero F, Marcus JH, Marongiu M, Maschio A, Del Vecchyo DO, Floris M, Meloni A, Delitala A, Concas MP, Murgia F, Biino G, Vaccargiu S, Nagaraja R, Lohmueller KE; UK10K Consortium, Timpson NJ, Soranzo N, Tachmazidou I, Dedoussis G, Zeggini E; Understanding Society Scientific Group, Uzzau S, Jones C, Lyons R, Angius A, Abecasis GR, Novembre J, Schlessinger D, Cucca F. “Height-reducing variants and selection for short stature in Sardinia.” **Nat Genet.** 2015 Nov;47(11):1272-81. doi: 10.1038/ng.3368 **(* joint first author)**

1c. Locke AE*, Steinberg KM*, **Chiang CWK***, Service S*, Havulinna A, Stell L, Pirinen M, Abel HJ, Chiang CC, Fulton RS, Jackson AU, Kang CJ, Kanchi KL, Koboldt DC, Larson DE, Nelson J, Nicholas TJ, Pietila A, Ramensky V, Ray D, Scott LJ, Stringham HM, Vangipurapu J, Welch R, Yajnik P, Yin X, Eriksson JG, Ala-Korpela M, Jarvelin MR, Manniko M, Laivouri H, FinnGen Project, Dutcher SK, Stitziel NO, Wilson RK, Hall IM, Sabatti C, Palotie A, Salomaa V, Laakso M, Ripatti S, Boehnke M, Freimer NB. “Exome sequencing of Finnish isolates enhances rare-variant association power.” **Nature.** 2019 Aug;572(7769):323-328. doi: 10.1038/s41586-019-1457-z **(* joint first author)**

1d. Jeon S, de Smith AJ, Li S, Chen M, Chan TF, Musken IS, Morimoto LM, Dewan AT, Mancuso N, Metayer C, Ma X, Wiemels JL†, **Chiang CWK†**. “Genome-wide trans-ethnic meta-analysis identifies novel susceptibility loci for childhood acute lymphoblastic leukemia.” **Leukemia.** 2022 Mar;36(3):865-

868. doi: 10.1038/s41375-021-01465-1. **(† joint corresponding author)**

2. Investigating the impact of fine-scale population structure and demography on genetic variation. It is through a deep understanding of the demographic history and population structure in the study population that we can design more robust genetic studies and analytic framework to elucidate the genetic architecture and evolutionary trajectories of disease risk alleles or of complex traits in a population. To this end, I have investigated the fine-scale structure and history of human populations known to have a unique past. For example, I characterized the fine-scale structure in Sardinia and found that the Sardinians deviate from current demographic model for the peopling of Europeans. I have also characterized the impact of population bottleneck on the distribution of deleterious variation in isolated Finnish populations. Similar lines of investigation have also been undertaken in the Han Chinese. In addition to empirical analysis, I am also actively developing integrative methods combining statistical and population genetic principles to better detect and visualize population structure. For example, I have developed a novel statistical framework to estimate genetic relatedness conditioned on genealogical trees across the genome, which overcome the bias due to marker ascertainment in the current standard of computing genetic relatedness, especially when incomplete genetic information is available.

2a. **Chiang CWK†**, Marcus J, Sidore C, Biddanda, A, Al-asadi H, Zoledziewska M, Pitzalis M, Busonero F, Maschio A, Pistis G, Steri M, Angius A, Lohmueller KE, Abecasis G, Schlessinger D, Cucca F, Novembre J†. "Genomic history of the Sardinian population." **Nat Genet.** 2018 Oct;50(10):1426-1434. doi 10.1038/s41588-018-0215-8 **(† joint corresponding author)**

2b. **Chiang CWK†**, Mangul S, Robles C, Sankararaman S. "A comprehensive map of genetic variation in the world's largest ethnic group – Han Chinese." **Mol Bio Evol.** 2018 Nov 1;35(11):2736-2750. doi 10.1093/molbev/msy170 **(† corresponding author)**

2c. Locke AE*, Steinberg KM*, **Chiang CWK***, Service S*, Havulinna A, Stell L, Pirinen M, Abel HJ, Chiang CC, Fulton RS, Jackson AU, Kang CJ, Kanchi KL, Koboldt DC, Larson DE, Nelson J, Nicholas TJ, Pietila A, Ramensky V, Ray D, Scott LJ, Stringham HM, Vangipurapu J, Welch R, Yajnik P, Yin X, Eriksson JG, Ala-Korpela M, Jarvelin MR, Manniko M, Laivouri H, FinnGen Project, Dutcher SK, Stitziel NO, Wilson RK, Hall IM, Sabatti C, Palotie A, Salomaa V, Laakso M, Ripatti S, Boehnke M, Freimer NB. "Exome sequencing of Finnish isolates enhances rare-variant association power." **Nature.** 2019 Jul 31. doi: 10.1038/s41586-019-1457-z **(* joint first author)**

2d. Fan C†, Mancuso N*, **Chiang CWK***†. "A genealogical estimate of genetic relationships" **Am J Hum Genet** 2022 May 4; 109(5):812-824. doi: 10.1016/j.ajhg.2022.03.016 **(* joint senior author, † joint corresponding author)**

3. Developing the framework to detect and characterize signals of polygenic adaptation. Natural selection is another important factor that contributes to our genomic pattern of variation and distribution of complex traits. In particular, polygenic adaptation is one likely mechanism through which a complex trait may evolve in human populations, but have only been extensively investigated in recent years. I demonstrated a putative genetic cause to the latitudinal difference in allele frequencies at height loci and showed that differences in height across mainland European and between mainland European and Sardinian populations may be due to polygenic selection. The polygenic signature for selection has motivated significant methods development in the field, and design and interpretation of the polygenic selection signature remain an intensive area of research. We also recently discovered that earlier studies of polygenic adaptation may be biased due to uncorrected stratification in analysis from large GWAS consortiums. To alleviate this concern, my current framework ascertains trait-associated loci from a geographically distant outgroup population to investigate signature of selection. Using this approach I continue to observe that differences in height between Sardinians and mainland Europeans are driven by natural selection. We are applying this framework to diverse understudied populations such as the Native Hawaiians and Latinos to understand if natural selection could underlie some of the excess risks in diseases such as obesity, type-2 diabetes, and childhood leukemia. Results of these research will provide a more complete picture of the evolution of complex traits in human populations.

3a. Turchin MC*, **Chiang CWK*,** Palmer CD, Sankararaman S, Reich D, Genetic Investigation of ANthropometric Traits (GIANT) Consortium, Hirschhorn JN. "Evidence of widespread selection on standing variation in Europe at height-associated SNPs." **Nat Genet.** 2012 Sep;44(9):1015-

9. doi: 10.1038/ng.2368. **(* joint first author)**

3b. Zoledziewska M*, Sidore C*, **Chiang CWK***, Sanna S*, Mulas A, Steri M, Busonero F, Marcus JH, Marongiu M, Maschio A, Del Vecchyo DO, Floris M, Meloni A, Delitala A, Concas MP, Murgia F, Biino G, Vaccargiu S, Nagaraja R, Lohmueller KE; UK10K Consortium, Timpson NJ, Soranzo N, Tachmazidou I, Dedoussis G, Zeggini E; Understanding Society Scientific Group, Uzzau S, Jones C, Lyons R, Angius A, Abecasis GR, Novembre J, Schlessinger D, Cucca F. "Height-reducing variants and selection for short stature in Sardinia." **Nat Genet.** 2015 Nov;47(11):1272-81. doi: 10.1038/ng.3368. **(* joint first author)**

3c. Sohail M, Maier RM, Ganna A, Bloemendal A, Martin AR, Turchin MC, **Chiang CWK**, Hirschhorn JN, Daly MJ, Patterson N, Neale B, Mathieson I, Reich D, Sunyaev SR. "Polygenic adaptation on height is overestimated due to uncorrected stratification in genome-wide association studies." **eLife.** 2019 Mar 21;8. pii: e39702. doi: 10.7554/eLife.39702.

3d. Chen M, Sidore C, Akiyama M, Ishigaki K, Kamatani Y, Schlessinger D, Cucca F, Okada Y, **Chiang CWK**. "Evidence of polygenic adaptation in Sardinia at height-associated loci ascertained from the Biobank Japan." **Am J Hum Genet**. 2020 Jul 2;107(1):60-71. doi: 10.1016/j.ajhg.2020.05.014.

4. Investigating the impact of Polynesian ancestry on complex traits in Native Hawaiians. Native Hawaiians are the second fastest growing, but also one of the most understudied, ethnic minority population in the United States. Prior to the 2000 U.S. census, Native Hawaiians and Pacific Islanders were aggregated with Asian Americans as a single racial group, thus masking the health disparities experienced by the Native Hawaiians and prohibiting extensive research with this population. We now know that compared to their European American counterparts, Native Hawaiians exhibit alarming rates of obesity, diabetes, cancers, and other related chronic health conditions, even after adjusting for common modifiable risk factors. To fill this gap of knowledge from a genetic perspective, we have demonstrated that genomic Polynesian ancestry proportion is significantly associated with increased BMI, decreased HDL, and increased risk for obesity, Type-2 diabetes, and congestive heart failure. While this association may in part capture cultural or environmental effects associated with Polynesian ancestry, it is also suggestive that there may exist Polynesian-specific alleles underlying these complex traits, and future genetic studies focusing on this population will be illuminating. Furthermore, we showed that current publicly available genomic resources are not yet sufficient for conducting successful genetic association studies in Native Hawaiians, though can be drastically improved even if just a small number of reference Polynesian individuals were whole genome sequenced for imputation.

4a. Sun H, Lin M, Russell EM, Minster RL, Chan TF, Dinh BL, Naseri T, Reupena MS, Lum-Jones A, Samoan OLaGA Study Group, Cheng I, Wilkens LR, Le Marchand L, Haiman CA, **Chiang CWK**. "The impact of global and local Polynesian genetic ancestry on complex traits in Native Hawaiians." **PLoS Genetics**. 2021 Feb 11;17(2):e1009273. doi:10.1371/journal.pgen.1009273.

4b. Lin M, Caberto C, Wan P, Li Y, Lum-Jones A, Tiirikainen M, Pooler L, Nakamura B, Sheng G, Porcel J, Lim U, Setiawan VW, Le Marchand L, Wilkens LR, Haiman CA, Cheng I, **Chiang CWK**. "Population- specific reference panels are crucial for the genetic analyses: an example of the *CREBRF* locus in Native Hawaiians." **Hum Mol Genet.** 2020 Aug 3;29(13):2275-2284. doi: 10.1093/hmg/ddaa083.

4c. **Chiang CWK**. "The opportunities and challenges of integrating population histories into genetic studies for diverse populations: a motivating example from Native Hawaiians." **Front Genet** 2021 Sep 27; 12:1687. doi: 10.3389/fgene.2021.643883.

Complete List of Published Work in MyBibliography:
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