Marshfield Clinic
Research Institute

University of California, Riverside

Dear Dr. Jeff Perry and Search Committee:

I am writing to apply for the open Tenure-track Assistant Professor Position in Epigenetics in the Department of Biochemistry, University of California, Riverside. I am extremely interested in this position where I believe my Ph.D and Postdoctoral training in human genetics, clinical epigenetics and bioinformatics will allow me to meet the challenge of precision medicine in which genetics, epigenetics and computational biology are combined to address important clinical problems. I view this position as an opportunity to apply my computational and wet-lab skills to develop a multi-faceted research program in precision medicine, investigating the interactions between genetic and epigenetic factors that underlie complex diseases. Currently, these interactions are underappreciated and poorly investigated. I am presently a Postdoctoral Research Fellow in the Center for Precision Medicine Research (CPMR) at the Marshfield Clinic Research Institute (MCRI) where I collaborate with Dr. Steven Schrodi working on (i) Developing and implementing new approaches to identify genetic and epigenetic variants/biomarkers involved in susceptibility, diagnosis, and prognosis of disease traits. Cancers and autoimmune diseases are of particular interest; and (ii) Functional assessment of genetic and epigenetic disease variants identified by GWAS and EWAS studies through the use of computational and biological approaches.

My formal academic training includes human genetics, epigenetics and bioinformatics. During my graduate program at Fudan University (2009-2015), I designed, conducted and participated in a series of genetic and epigenetic epidemiology studies of cancer and autoimmune diseases. In these projects, I led numerous aspects including study design, data collection, data analysis, and manuscript preparation. This experience provided me with considerable training in both computational and molecular genetics. For example, I applied a multi-machine learning algorithm approach to identify optimized lung cancer diagnostic panels by combining multiple publicly-available genome-wide DNA methylation array datasets and then translating these results by developing a low-cost methylation genotyping assay, MSD-SNuPET, to detect the methylation status for ~30 loci in 500 samples simultaneously.

In 2015, I accepted a position at the University of Texas Health Science Center at Houston to complete the remaining projects initiated during my exchange scholar program between Fudan University and UThealth (2013-2015). I developed a novel functional principal components analysis to accelerate the analysis of high-dimension data including NGS data and image data. In addition, I made important contributions to RNA-seq data processing including raw data calling and created solutions to big data storage. These studies were published in 2015.

In the middle of 2015, I joined the Postdoctoral program in the Department of Bioengineering, University of California, San Diego, where I conducted a project in which I proposed the concept of a methylation haplotype load (MHL) to quantify both methylation level and haplotype complexity simultaneously and to infer the tissue-of-origin for circulating cell-free DNA methylation signals. My study demonstrated MHL is a powerful metric to estimate the methylation signals in cell-free DNA compared with the traditional methylation level, methylation entropy, or epi-polymorphism. In summary, my work provided a new approach to apply cell-free DNA methylation to serve as an effective biomarker for tissue-of-origin mapping in cancer screening. The study was published in *Nature Genetics* and I was the lead author.

At the end of 2017, I was recruited to the Center for Precision Medicine Research at the Marshfield Clinic Research Institute (MCRI). At MCRI, I leveraged my computational and biological skills to identify novel disease genes within the 20,000 sample Personalized Medicine Research Project using exome-chip data. I implemented a novel genetic model to discover combinations of recessively-acting susceptibility variants for 15 complex diseases. The study identified a novel hemochromatosis gene, *FGF6*, and I conducted a series of protein-protein network analyses and molecular evolution analysis, providing strong evidence supporting *FGF6* being involved in iron overload. Subsequently, I designed functional studies to assess additional evidence for the role of Fgf6 in iron metabolism. The study was published in *Blood* this year and I was the lead author.

Overall, I think, my multidisciplinary training in human genetics, epigenetics and bioinformatics will enable me to build a highly productive laboratory on the development and implementation of novel molecular diagnostic and prognostic approach to genetic diseases and human cancers, especially cell-free DNA based non-invasive approaches for cancer and other diseases. I would enjoy discussing this position with you in the weeks to come. Please don't hesitate to contact me if you require any additional materials or information. Thank you very much for your consideration.

Sincerely,

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