25 October 2018

Re: Tenure-track Faculty in Human Genetics and Genomics
Department of Medical Genetics
University of Wisconsin-Madison

Dear Search Committee:

Please consider my application in response to the open Tenure-track Faculty position in Human Genetics and Genomics at UW-Madison. Currently, I am an Associate Research Scientist within the Center for Human Genetics at the Marshfield Clinic Research Institute where my laboratory investigates (i) the genomics of immune system pathologies, metabolic dysfunction, host response to infection and developmental disorders, (ii) theoretical disease genetics, and (iii) statistical genetics.

My formal training is in theoretical population genetics and statistical genetics. As a graduate student, I developed stochastic processes to model molecular evolution dynamics focused on DNA substitutions. I started my professional career in 2000 where I led a large-scale computational effort to identify colon cancer genes in the Utah population under Raymond White. Concurrently, I headed an autoinflammatory disease mapping effort. Later, I accepted a position at Celera where, in 2003, I designed and analyzed the first exome-wide disease association study using 30,000 putative functional variants which led to the discovery of the missense polymorphism R620W segregating in the protein tyrosine phosphatase gene, *PTPN22* in significant association with rheumatoid arthritis. Additionally, I led all fine-mapping efforts at Applied Biosystems/Celera, which resulted in the first identification of *TRAF1* haplotypes contributing to rheumatoid arthritis susceptibility. Subsequently, I led a psoriasis mapping study in 2006 which discovered the *IL23R*, *IL12B,* and *IL13* genes as predisposing factors to psoriasis. These results aided in solidifying the Th17 dysfunction model for these pathologies. I am an inventor on seven US patents describing these results in the context of genetic-based diagnostic panels. During this time, I also continued my research into statistical genetics methods for disease gene studies where I (i) was the first to produce a close-form solution for a Bayes Factor testing genetic association with disease status, (ii) developed the theory for linkage disequilibrium patterns under disease models, (iii) originated a novel approach using statistical power as a metric to identify sets tagging SNPs, and (iv) developed a Bayesian network approach using measures from information theory to prognose disease states.

In 2010, I accepted a position at the Marshfield Clinic Research Institute. My research program at the Center for Human Genetics involves several experimental studies using a variety of approaches to map disease genes, work on disease genetics theory, and statistical genetics. My lab is currently conducting studies investigating the genomics of 1) molecular intermediate phenotypes for chronic, systemic inflammation, 2) autoimmune diseases, 3) metabolic dysfunction, 4) iron metabolism disorders, and 5) host response to pathogens. These studies have utilized a variety of novel genetic approaches including gene-based, recessive diplotype scans and shared chromosomal region analyses. Our theoretical disease genetics studies have been focused on genetic architecture of complex diseases and the decay of disease association with declining linkage disequilibrium from causal sites. Lastly, our statistical genetics work has examined both Bayesian and frequentist approaches to multiplicity, probabilistic methods to hypothesis testing, permutation routines, and linkage methods applied to extended kinships. My objective is to continue to grow my research program at UW-Madison, employing my expertise in human genetics and statistical/theoretical genetics to understand the genetics and molecular pathogenesis of systemic inflammatory diseases. I envision a program fully funded by external sources. Additionally, I have a strong interest in teaching genetics, particularly material focused on disease gene mapping experiments, theory and interpretation of genetic data at both the undergraduate and graduate level. Notably, over the past eight years I have

spent over 9,000 hours mentoring other tenure-track faculty, postdoctoral fellows, physicians and summer students at the Marshfield Clinic.

I view the environment and focus at the Genetics Department at UW-Madison to be well-aligned with my research and career aims. For decades, I have strongly felt that research designed to understand the etiology of complex diseases for the ultimate purpose of remediation of those conditions is exceedingly important as efficacious therapeutic intervention will yield enormous benefit for those patients. I have ongoing collaborations with UW-Madison Professors Judy Smith, Miriam Shelef, and Mark Craven. Further, my collaboration with Professors Janet Lainhart and Andy Alexander at the Waisman Center on neuroimaging genetics has been extraordinarily fruitful. I view this faculty position as an opportunity to further expand the synergistic research efforts with my UW-Madison colleagues. Moreover, the functional biology expertise at UW and the computational resources opens numerous complementary research avenues.

Please do not hesitate to contact me if you have any questions.

Sincerely,

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