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12 December, 2005

Dr. Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142, 1001 E 3rd St.
Bloomington, IN 47405-7005

Re: **Huiying Li**

Dear Dr. Brun:

Dr. Huiying Li is a "must interview" candidate for assistant professorships in bioinformatics. She is extremely bright, very broad in interests, highly effective, creative, confident, and charming. Her scientific background includes metabolic studies prior to coming to UCLA; protein expression, purification, crystallization, and X-ray structure determination in my group; statistics and scientific programming; and bioinformatics both of protein interactions from genome sequences and of patient-derived DNA microarrays. Her notebooks are a pleasure to see: far closer in appearance to Leonardo's than to mine. All of her reasoning is set out, as well as her results. She speaks and writes beautiful English, and has speaking command of 5 other languages. Her explanations are so clear, she won one of the coveted UCLA Chemistry/Biochemistry teaching awards. She is without doubt one of the two strongest graduate students of the more than 60 I have supervised in the past 36 years.

Huiying is able in both experimentation and bioinformatics, and I foresee her engaging in both experimental and computational work in the long run, as she moves towards her goal of illuminating the fundamentals of cancer. But in the short run, she wants to work in bioinformatics.

Huiying's achievements here started with crystal structures of metabolic enzymes. She then devised a new computational method of detecting parallel pathways and complexes in cells from analysis of comparative genomes. Once started in bioinformatics, she became interested in medical applications, and formed a collaboration with my colleague Robert Modlin of our medicine department. Her data analysis of his microarrays was so illuminating that she elevated one study to a Science paper of which he made her co-first author, and he volunteered to pay her salary from that moment on.

At our group meetings and journal club, Huiying speaks up with penetrating insights, all modestly offered. She is one of those rare scientists who make work seem easy. In the years she has worked with me, I have never seen her in any mood other than one of cheerful thoughtfulness, and every conversation with her is rewarding. She will make a valued faculty colleague in all respects, and is someone from whom I expect important discoveries in the years ahead.

Sincerely,

David Eisenberg

David Eisenberg
Director, UCLA-DOE Institute for Genomics and Proteomics
Professor, Dept. of Chemistry and Biochemistry & Dept. of Biological Chemistry
Investigator, Howard Hughes Medical Institute

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December 19, 2005

Dr. Yves Brun
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Dear Dr. Brun,

It is my great pleasure to write this letter in support of Dr. Huiying Li's application for a faculty position at your institution.

I have known Huiying for three years as a student in Dr. Eisenberg's lab. Our lab was investigating leprosy as a model to understand the human immune response to microbial pathogens. For a long time, we were investigating the role of one immune gene at a time in its pathogenesis. However, gene microarrays allowed us to study over 30,000 genes at a time. However, we found that we could not interpret the large amount of data one gets when doing this kind of experiment.

Huiying to our rescue by applying bioinformatic and statistical methods to the gene expression data and has made significant discoveries. She successfully distinguished two clinical forms of leprosy by identifying the gene expression patterns. This was extremely exciting because the clinical manifestations found in leprosy form a spectrum and the disease types are hard to distinguish by traditional methods. The treatments of different types of leprosy are also very different. Therefore, it is very important to be able to discriminate different forms of the disease. From the data analysis, Huiying also discovered that one patient sample was misdiagnosed based on the tissue biopsy. This shows that her method has great potential in accurately diagnosing infectious disease and thus eliminating human errors using nonobjective criteria. This work is one of the first studies of its kind in which gene expression profiling distinguished immune disease types, leading to new ways to diagnose and determine the best course of treatment. The work on leprosy has been published in the journal of ***Science***, one of the most prestigious journals in sciences. Dr. Huiying Li's contribution was vital for this project's success. Based on her work, we successfully obtained a five-year grant from the National Institutes of Health to continue study of host immune response in leprosy.

Dr. Huiying Li continued to show that she is a gifted scientist by designing new computational methods to analyze data from large-scale DNA microarray experiments. She devised two-way ANOVA analysis and one-way ANOVA analysis to analyze the gene expression pattern in stimulated monocytes and dendritic cells, which mimic the immune responses in tuberculosis (TB) patients. Being one of the first few scientists to apply these statistical methods on genomic scale in medical research, she discovered a new significant role of vitamin D in defending against bacterial infection. We have shown that African-Americans have significantly decreased vitamin D levels due to less UV absorption in darker skin and decreased milk consumption. And it has long been known that the susceptibility of African-Americans to tuberculosis is greater than that of Caucasians. Huiying's discovery also provides new scientific basis for the historical understanding of tuberculosis treatment by sunbathing. The demonstration of UV light is beneficial to TB patients earned Danish physician, Niels Ryberg the Nobel Prize in 1903. Dr. Huiying Li's finding suggests that adding vitamin D in food supplement can be a modern therapeutic approach for populations that may lack enough vitamin D. The manuscript of this work is being reviewed for ***Science***. It is no doubt that Huiying's research has contributed to a new understanding of the host defense to medical pathology.

In addition to the two papers mentioned above, we also published a paper together on the role of IL15 in immune response in the journal of ***Nature Medicine***, the top journal in medical science. Another three papers are also in preparation for publishing.

I believe that Huiying Li will continue to make great contributions to the field of life sciences and medical research. Personally, I would rank Dr. Li among the top 1% young scientists I have interacted with in my more than 20 years' medical research career. Her remarkable creative talent and intellectual skills are tremendous assets. Therefore, with my strongest enthusiasm, I respectfully request that Huiying be appointed a faculty position with your institution.

Sincerely,

Robert L. Modlin, M.D.
Klein Professor of Dermatology,
Professor of Microbiology and Immunology
and Molecular Genetics
Chief, Division of Dermatology,
Vice Chair for Cutaneous Medicine and Dermatological Research