THE ROCKEFELLER UNIVERSITY
1230 YORK AVENUE · NEW YORK, NEW YORK · 10021-6399

Leslie Vosshall, Ph.D.
Chemers Family Assistant Professor
Laboratory of Neurogenetics & Behavior
1230 York Avenue · Box 63
New York, N.Y. 10021-6399
Phone: 212-327-7236
Fax: 212-327-7238
E-mail: leslie@mail.rockefeller.edu

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

October 4, 2005

Dear Colleagues:

I write to give my unqualified support of **Dr. Yun Zhang**'s application for a tenure-track assistant professor position in your department. Yun is doing some of the most creative and compelling work in behavioral neuroscience that I know of and I believe she is a very strong candidate for this position.

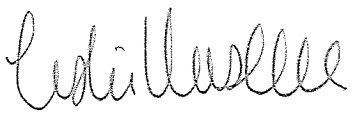
I have known Yun for a bit less than one year, since she moved with Cori Bargmann from UCSF. Cori has a large and impressive group, with many smart students and postdocs. Even among this competitive crowd, Yun stands out as particularly intelligent, effective, and collegial scientist. She gave an excellent presentation at one of our monthly group lab meetings and I have followed the progress of both of her postdoctoral Nature papers carefully. Her work has demonstrated that *C. elegans* can recognize the smell of pathogenic bacteria and that they can learn to avoid these stimuli once exposed to them. Many investigators have tried to study learning in this primitive nematode, but used paradigms that were not "relevant" to the worm. Yun has shown that by careful consideration of the natural ecology of these animals, clever experiments can be designed to crack the learning problem in this genetically manipulable animal. I have read Yun's faculty research proposal and can attest that she has thought carefully about the next steps and is well on her way to a strong independent career as a neurobiologist. Preceding her spectacular performance in the Bargmann lab was a tour-de-force graduate career in Marty Chalfie's lab at Columbia. Yun spearheaded amazing microarray experiments which involved identifying the transcriptional profile of purified *C. elegans* touch neurons.

You may know that we are launching our own faculty recruiting effort at Rockefeller this season, paying particular attention to increasing the representation of junior women on our faculty. Yun to me represents that rare commodity that combines both scientific and personal excellence. First, she has excelled scientifically both in her PhD and postdoctoral training. Second, she has

been effective and efficient in finishing her training promptly. Third, she combines a lovely personality with an obvious enthusiasm for science. Fourth, she is an effective communicator and I expect will make an excellent lecturer for students. Finally, her proposed field of independent research will be popular among PhD students, postdocs, and funding agencies.

I think she will be a strong contender in the job market this year and I urge you to give her application the most serious attention. I give her my highest recommendation.

Very truly yours,



Leslie B. Vosshall, Ph.D.

HHMI
HOWARD HUGHES MEDICAL INSTITUTE

October 12, 2005

To the search committee:

I am writing in enthusiastic support of Yun Zhang's application for a faculty position at Indiana University. Yun is a postdoctoral researcher who has been in my lab for three years. She has established an exciting and creative research area during this time, and she is an outstanding candidate for a faculty position.

In my lab, Yun developed a convincing, physiologically relevant assay for olfactory learning in the nematode *C. elegans*. *C. elegans* is a powerful organism for genetic studies, but its behavior is relatively simple. There are a few learning paradigms (the best is for learning temperature) but we have not been happy with our ability to induce olfactory learning. Yun showed that if she challenged an animal with an ecologically relevant task – the ability to distinguish between pathogenic and non-pathogenic bacteria – the worm was able to learn about the odors. Using clever multiple-choice maze assays, she showed that the trained worms specifically learned to avoid the pathogen that they had encountered, but not other bacterial strains. Moreover, Yun is making progress on understanding the mechanism of learning at a circuit level. She has implicated the modulatory transmitter serotonin in learning, and shown that specific neurons increase serotonin synthesis after infection by pathogens. This work is in press as an article in *Nature*.

Using her behavioral assays, cellular analysis, and genetics, Yun should be able to dissect the mechanisms for generating a specific olfactory memory: the association of the odor of a food with a pathogenic infection. This will be a major step forward for the field. I think this is some of the most significant work in my lab right now, but since Yun built this system from its inception, the pathogen-learning problem will be hers to study and I will not compete with her.

In a second collaborative project, Yun has worked with Jonathan Ewbank at Marseilles to discover how *C. elegans* recognizes a specific natural product from a pathogenic bacterium. Yun traced the response to one class of olfactory neuron that helps the worm evade the pathogen. A paper on this work has been submitted.

Yun is an outstanding postdoc. Her project required skill, creative insight, and a new way of thinking about the problem. Basically, before Yun began to think about olfactory learning, we and other people in the field were always studying pure odors; she was the first to use the more complex odor of natural bacterial food. Much of scientific success just comes from asking the right question. Yun has the ability to find the question to ask.

Yun is a technically creative and innovative scientist. This has been apparent at many stages of her project. All of our previous studies of olfaction had used relatively simple two-odor choice assays. Yun wanted to make finer discriminations, so together with an engineer in the lab, she microfabricated environmental chambers for *C. elegans*-scale mazes with many choices of bacterial odors. The mazes are proving to be very powerful for distinguishing

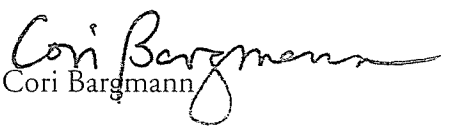
Cori Bargmann, Ph.D.
Investigator
Torsten N. Wiesel Professor

The Rockefeller University
Laboratory of Neural Circuits and Behavior
1230 York Avenue, New York, New York 10021
212.327.7241 • Fax 212.327.7243 • cori@rockefeller.edu

between different models for learning. Yun has been innovative throughout her career. She came to my lab following graduate work with Marty Chalfie at Columbia University, where she performed a spectacular piece of work on mechanosensation. Yun wanted to reach a complete understanding of the molecular biology of the mechanosensory neurons. She was the first person to solve a problem in single-neuron genomics in any system. She developed ways to isolate and sort mechanosensory neurons from embryos using a specific GFP marker, then worked out techniques for microarray analysis with small amounts of pure RNA from the sorted cells. Ultimately Yun was able to generate an extensive analysis of the neurons that appeared as a Nature paper with Yun as first author. It's a sign of her talent that she's done original and exciting work both as a student and as a postdoc.

At every stage of her career, Yun has shown enormous drive and intellectual boldness. She is the best kind of scientist: enthusiastic, creative, motivated, thoughtful, rigorous, and collaborative. She has my strongest support.

Sincerely,



Cori Bargmann

COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK
DEPARTMENT OF BIOLOGICAL SCIENCES

October 10, 2005

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

Dear Dr. Brun,

I strongly recommend YUN ZHANG for your Assistant Professorship. Yun, who is now a postdoctoral fellow in Cori Bargmann's laboratory, accomplished a remarkable piece of work while in my lab as a graduate student. We were interested in developing molecular methods of obtaining genes expressed in the *C. elegans* touch cells. We had had some success using Representational Difference Analysis, and Yun decided to use this subtraction method to compare cDNAs from animals with differentiated touch cells (wild type) or differentiation-defective touch cells (*mec-3*). She worked very hard (including, e.g., analyzing a set of 700 candidate clones), but was only able to find one new touch cell-expressed gene, which she characterized (the paper on this research was published in *Mechanisms of Development*). All-in-all she spent a couple of very frustrating years trying to combine this subtraction method with DNA arrays, but could never produce consistent results. She concluded, correctly, that the method was not sensitive because it used RNA from whole animals. After talking with a postdoc in the lab, she decided that she would try to isolate the touch cells from embryos with wild type or mutant touch cells, and make RNA from them. Working essentially on her own, she got the culturing methods working (they had been developed by others), modified them to optimize the number of GFP-labeled touch cells, searched the literature for an appropriate collaborator with whom to do the cell sorting (Tom Delohery, then at Memorial Sloan Kettering), and collaborated with him to produce the cells. All of this effort produced a collection of about 4 million cells at 50% purity. She then isolated RNA and worked out problems with the linear amplification procedure previously developed by Jim Eberwine at Penn to amplify the RNA about one million-fold. She then went to Stanford and did the DNA array experiments in Stuart Kim's lab. The result of all this work was a gold mine. Using statistical methods she found a collection of 71 *mec-3*-dependent genes. These included nine of the ten known genes of this class. In addition, Yun showed that the top gene on her list was a previously uncloned touch gene, *mec-17*. Several other genes encode proteins that are tantalizing, including one potassium channel, a GABA A-

SHERMAN FAIRCHILD CENTER FOR LIFE SCIENCES
1212 Amsterdam Avenue New York, NY 10027

COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK
DEPARTMENT OF BIOLOGICAL SCIENCES

like receptor, some T-complex chaperonins, and several enzymes. In addition she collaborated with a new faculty member in our department, Harmen Bussemaker, to do a bioinformatics description of her results. This beautiful set of experiments was published in *Nature*.

Yun's procedure was an astonishing breakthrough, because it allowed the power of DNA arrays and whole genome analysis to be used at the level of single cell types. Before Yun's work two papers had been published using DNA arrays in *C. elegans*, one looking at differences in germ line expression (the germ line makes up most of the animal) and the other looking at differences at different development stages. Yun's work has and will keep us busy for many years. It also showed the way for similar experiments in *C. elegans* and other organisms.

As this brief description of her efforts points out, Yun is a very resourceful and determined scientist, who can bring together and develop diverse techniques to accomplish her goals. She has continued to be successful as a postdoc with Cori Bargmann. Past experiments into learning using *C. elegans* have been difficult and not very informative. Yun's development of an experimental system involving olfactory avoidance looks very promising and has already produced important results. I feel she is a very strong candidate for your position.

Sincerely,

Martin Chalfie

Martin Chalfie, Ph.D.
William R. Kenan, Jr. Professor of Biological Sciences

SHERMAN FAIRCHILD CENTER FOR LIFE SCIENCES
1212 Amsterdam Avenue New York, NY 10027