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December 15, 2005

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

Dear Dr. Brun:

I am writing to you at the request of **Mara C. Duncan,** Ph.D., in support of her application for the faculty position you currently have available. Mara has been conducting postdoctoral research with Professor Gregory S. Payne in the Department of Biological Chemistry at the UCLA School of Medicine since 2001. Greg himself was a Ph.D student with Harold Varmus at UCSF and then a postdoc here at Berkeley with my friend and colleague, Randy Schekman, in the late 1980's. Greg has been at UCLA for quite some time now and has been a solid contributor to the vesicular trafficking field, especially with regard to processes and mechanisms at the Golgi compartment. I'm sure your colleagues in this research area are very familiar with Greg's work.

In any event, I have known Mara since the time she was admitted to graduate study here at Berkeley in Fall, 1995. I taught a graduate course (MCB 230) in molecular cell biology that Mara took in her first year. Also, I was a member of Mara's Oral Qualifying Examination Committee in her second year. Thereafter, I was a member of her Annual Thesis Guidance Committee (ATGC), and a Reader and signatory of her doctoral dissertation (filed May, 2001). Hence, I feel that I am able to comment quite knowledgeably about Mara's potential, capabilities, and accomplishments.

Mara came to Berkeley from the University of Washington, Seattle, where she conducted undergraduate research and received a very strong background in the biological sciences. In my course, Mara was, without doubt, the ablest and most intellectually gifted of the more than three dozen graduate students in the class. Mara carried out her thesis work in the laboratory of my colleague and friend, Professor David G. Drubin. Initially, Mara was stymied by a lack of technical facility at the bench. Sometimes even routine manipulations (cloning, protein purification, etc.) didn't come easily to Mara. However, due to her commitment, energy, and perseverance, she managed to do, first, quite a niece piece of work on a yeast WASp homolog, Las17/Bee1. Her genetic studies on her Las17 mutants, and some sequence gazing, then led her to predict that Pan1, a protein of previously unknown (or, more correctly, improperly assigned) function, would also, like Las17, bind and activate the Arp2/Arp3 complex to promote actin filament assembly. Moreover, her work provided

strong evidence that Las17- and Pan1-dependent Arp2/Arp3 recruitment and actin filament formation are critical for a clathrin-independent route of endocytosis in yeast. These findings were published in a very nice paper that was an important advance in this field [See: Duncan MC, Cope MJ, Goode BL, Wendland B, Drubin DG (2001) Yeast Eps15-like endocytic protein, Pan1p, activates the Arp2/3 complex. Nature Cell Biol. 3: 687-690]. Mara's skill at the bench improved a lot over the years that she spent in the Drubin Lab. In fact, she contributed significantly to the refinement of procedures for recovering in good yield GST-fusion proteins expressed in yeast [See: Rodal AA, Duncan M, Drubin D (2002) Purification of glutathione S-transferase fusion proteins from yeast. Methods Enzymol. 351: 168-172]. Based on her productivity as a postdoc since she joined the Payne Lab, and her recent success with chemical genetic approaches and high-throughput screening methodology, I think it is fair to say that the level of her technical facility is now equivalent to that of the most innately skillful experimentalists.

Mara succeeds because she is extremely bright and always willing to make the extra effort that is needed to bring a project to fruition. Moreover, whenever she chatted with me as a student or more recently at meetings (for example, the Yeast Cell Biology Meeting at the Cold Spring Harbor Laboratory this past summer), she always seems to be lively, inquisitive, open to new ideas and suggestions, and receptive to constructive criticism. She is invariably interested in a broad range of subjects in biology and is quite well-read. I think her choice of Greg Payne's lab for her further training was a wise one because it provided her with ample opportunity to further hone her skills in biochemistry and cell biology. I think that your program in the Dept. of Biology at the University of Oregon would be an especially attractive place for her to commence her independent career because she has the potential to synergize with and complement other scientists there whose work impinges on vesicular trafficking, both in yeast and/or in animal cells. Moreover, her recent hands-on experience with chemical library screening and high-throughput bioassays would also make her a distinct asset to any new programs you may have in Chemical Biology or any other new initiatives you may have that acknowledge the burgeoning of the interface between chemistry and biology.

In summary, Mara is an exceptionally bright, exceedingly well motivated, very hard-working and technically proficient young investigator. I would placed her in the top 10% of all of the graduate students who have matriculated from Berkeley during my now 32 years on the faculty of this university. I am absolutely certain that Mara's initiative and productivity will carry over into any area of biomedical research to which she sets her mind. For these reasons, I am convinced that Mara warrants your most serious consideration.

Sincerely yours,

Jeremy W. Thorner
Professor of Biochemistry and Molecular Biology

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December 14, 2005

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

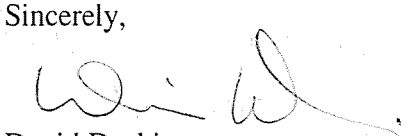
Dear Prof. Brun:

I am writing to provide my enthusiastic support for the candidacy of **Mara Duncan** for the faculty position being offered in your department. Mara was a graduate student in my laboratory, studying the molecular mechanisms by which endocytic proteins harness actin assembly forces for endocytic trafficking events. She is one of the brightest and most scientifically engaged students to have passed through my lab. Not only was she a major intellectual force behind her own studies, but she also provided other members of the lab with many excellent ideas for scientific directions in their projects. Mara's intellect was most obvious during lab meetings. She asked penetrating and critical questions when other members of the lab were presenting their data. Her level of sophistication and the depth of her insights were truly impressive.

Mara's project involved studies of activators of the yeast Arp2/3 complex, and their endocytic functions. In budding yeast, actin assembly mediated by the Arp2/3 complex is strictly required for endocytic internalization. To Mara's surprise, mutation of the Arp2/3 activating domain of the yeast WASP, Las17, surprisingly had no effect on endocytosis. This was highly unexpected because no other Arp2/3 activators were known at the time. Mara noticed that the endocytic protein Pan1 had sequences resembling those in the Arp2/3 activation domain of Las17. She hypothesized that Pan1 might be a novel Arp2/3 activator, and that this activity might be redundant with that of Las17. Using an elegant combination of biochemistry, genetics and cell biology, Mara proved her hypothesis to be correct. Her paper on this work in *Nature Cell Biology* has been a cornerstone for many of my projects since she left the lab. I credit this excellent piece of work to Mara's keen intellectual abilities since she is the one who posited the hypothesis that motivated the project.

I have followed Mara's progress as a postdoctoral fellow closely. She has been adventurous with the approaches she has chosen, and has been very productive. She seems to have fully hit her stride as an experimentalist. Mara has all of the capabilities that are required of a successful, independent research scientist. She thinks deeply and clearly, she is highly inquisitive, and she is highly motivated. Mara's presentations were always extremely clear. For this reason, I believe that she will be an excellent teacher. I recommend her to you strongly and without reservation.

Sincerely,



David Drubin
Professor and Division Head