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3 October 2005

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

Re: Richard Gardner, Ph.D.

Dear Dr. Brun,

I highly recommend Richard Gardner for the position in your department. I can say without hesitation that rich is one of the best and most mature postdoctoral fellows that I have been associated with. He has all the qualities of a first rate scientist.

I have known Rich for the past three years and have been able to observe him at the bench as well as in seminars, journal clubs and daily discussions.

Rich's qualities as a scientist can be seen from how he has carried out his main project, protein quality control in the nucleus of S. cerevisiae. Reasoning that mutants of a putative nuclear quality control system might show up as suppressors of ts mutations in multiple, independent genes encoding nuclear proteins, he searched the literature and came up with San1 whose deletion suppressed ts alleles of three distinct genes. Rich subsequently demonstrated that San1 encodes a nuclear localized ubiquitin ligase. He has since characterized several other substrates for San1 and demonstrated a phenotype for san1 mutants. I believe that this has been the first demonstration of a specialized, nuclear, protein quality control system. More recently, Rich has characterized mutants that are dependent on active San1 for viability. He has also characterized mutants that cannot survive in the absence of active San 1 in which the mutated San I substrates form large aggregates in the cell nucleus. He thus has developed a yeast model for diseases caused by protein aggregation. At present he is attempting to identify other components of the nuclear quality control apparatus. Some of these were preliminarily identified in his initial search "in silico". He has also developed genetic selections for others.

In the future, Rich would like to expend his studies to higher organisms. He has a very interesting model that some of the codon expansion diseases could result from the failure of the protein quality control systems to degrade the long repeats of the same amino acids. Presently he is trying to establish a model system in yeast with San1. Since San1 is conserved, this appears to be a very interesting avenue of exploration.

Rich is accomplished at both biochemistry and genetics. I have been very impressed by his level of organization and his work ethic. He is both highly intelligent and imaginative. His interests are extremely broad and his knowledge encyclopedic. He expresses himself very well and has the patients to explain things to even the least initiated. This brings up his willingness to help others and his kindness. I am sure that he will make an excellent colleague.

All in all, it is difficult for me to imagine a better candidate than Rich.

Sincerely,
Harvey Eisen

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September 20, 2005

Dear Faculty Search Committee,

I am writing with my highest recommendation for Dr. Rich Gardner, a candidate for your faculty search. Rich is currently a postdoctoral fellow in Dan Gottschling's lab and I have interacted with him extensively during our time here due to our common scientific interests. Rich has done truly outstanding and groundbreaking work in Dan's lab. He has shown that budding yeast have a ubiquitin-mediated proteolysis pathway in the nucleus that degrades aberrant proteins and termed this "nuclear quality control". This is highly significant because it is the first demonstration of such a mechanism in any organism and is likely to be conserved. The entire idea of looking for nuclear quality control was Rich's idea that he brought to Dan's lab. He hypothesized that the nucleus would contain a quality control degradation system and realized that mutants in this system might suppress temperature sensitive yeast mutants by preventing their degradation. He did an extensive literature search and discovered a ring finger protein called San1 that had the property of suppressing a variety of temperature sensitive mutants. Rich then did all the key experiments to show that San1 is indeed a ubiquitin ligase that degrades aberrant nuclear proteins. Strikingly, he was able to show that San1 targets aberrant proteins but not the wild type versions, proving that it really is a quality control pathway. This work was published in *Cell*. Rich is now trying to identify additional components and substrates of the nuclear quality control pathway. To this end, Rich is developing a strategy to purify all the ubiquitinated cellular proteins and identify them by mass spectrometry. He will then be able to identify San1 targets by looking for proteins that are not ubiquitinated in a *san1* mutant strain. Once he has developed these techniques, he will be able to apply them to other ubiquitin pathways to further develop his interests in other cellular degradation systems. This work is highly relevant to diseases such as Huntington's Disease where aggregated nuclear proteins are implicated in disease progression and will provide another system for him to elucidate the molecular details of nuclear quality control. The truly amazing thing is that Rich has worked on projects in

addition to nuclear quality control. Without going into great detail, Rich also published an *MCB* paper describing the mechanism of gene silencing at telomeres by the Ubp1 ubiquitin protease. To have produced this amount of quality work is a true testament to Rich's dedication and interest in science.

Rich is a fantastic colleague and I think that he would be a great asset to any department. He is a natural scientist- he has a genuine curiosity about things and asks great questions about other people's science. He attends our lab meetings just to have more extensive contact with other labs and learn about other biological processes. He always makes great suggestions and is truly interested in everything going on around him. He is also a wonderful colleague. Our lab found a kinetochore protein that was degraded by ubiquitin-mediated proteolysis and Rich was extremely generous with advice and reagents to help guide this project. Rich has already demonstrated the ability to have original and creative ideas and can carry them through to fruition. I cannot say enough about his potential abilities to be a Principal Investigator. He has the drive, motivation and creative spirit to be a huge success. In sum, I give Rich my highest recommendation and hope that you consider him a top candidate for your faculty position. Please let me know if you have further questions.

Sincerely,

Susan Biggins

Sue Biggins, PhD
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