

10/28/05



SALK INSTITUTE
FOR BIOLOGICAL STUDIES

Jeremy Bennett
Faculty Search Coordinator
Department of Biology
Indiana University
1001 East 3rd Street, Jordan Hall 127
Bloomington, IN 47405-3700

Dear Dr. Bennett,

It gives me great pleasure to be able to strongly recommend Xuelu Wang for a faculty position at your institution. Xuelu has been carrying out biochemical and genetics studies of brassinosteroid action in Arabidopsis in the laboratory of my colleague Joanne Chory at the Salk Institute. I have known Xuelu for ~ 3 years. Since Joanne's and my laboratories share the same floor and have joint lab meetings, I have been able to closely observe Xuelu's scientific progress. In short, I have been very impressed by him. Xuelu was very highly recommended by Brian Larkins (Arizona) where he was a Ph.D student. Upon joining Joanne's group, he had the opportunity to participate in any of a variety of ongoing projects including chloroplast/nuclear interaction, brassinosteroid biosynthesis/signaling, natural variation, or light signal transduction. For his postdoctoral research project, Xuelu chose the very challenging and highly competitive area of receptor protein kinase/substrate interaction in steroid signaling. Never-the-less, Xuelu has made outstanding progress toward bettering our view of BRI action and in particular receptor function and targets. Xuelu has aggressively focused on understanding the mechanism of activation of BRI1.

As outlined in his research plan, Xuelu has discovered a BRI-interacting protein called BKI1. Using several assay systems, he has found BKI1 is very likely a substrate of BRI1 kinase and is an early component involved in brassinolide signaling. His other main project is the dissection of the BRI1 kinase. He has done extensive analysis of this protein and has made significant inroads into understanding the biochemical mechanisms of protein activation. He has already published a significant study in *Developmental Cell*.

I fully expect that Xuelu will continue to demonstrate a high level of creativity and believe that he would most certainly be an asset to your department. I have found Xuelu to be highly interactive. He is always willing to talk about the results of his latest experiments and also, he is a good listener. I don't think you can go wrong by inviting him out for a seminar to see if he is a good fit for your position.

Sincerely,

A handwritten signature in cursive script, appearing to read "Joseph R. Ecker".

Joseph R. Ecker
Professor

October 27, 2005

Jeremy Bennett
Faculty Search Coordinator
Department of Biology
Indiana University
1001 East 3rd Street
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Dear Members of the Search Committee:

re: Dr. Xuelu Wang

I am writing in very strong support of Dr. Xuelu Wang's application for your position. Xuelu has been a HHMI-funded postdoctoral fellow in my lab during the past 3.5 years, working on the plant steroid hormone signaling project in my lab. Xuelu has taken on the challenge of defining the mechanism of activation of the steroid receptor, BRI1, and has made admirable progress. Xuelu is very bright and a real lover of science. He is an expert biochemist, molecular biologist, and plant geneticist, as well as a valued colleague. I'd rank him in the top tier of the excellent postdoctoral fellows I have known in Plant Biology in the La Jolla area over the past 17 years. I most enthusiastically support him in his career goal, which is to start his own academic laboratory studying the molecular mechanisms of steroid signaling in plants. Because only a few signaling systems are well-defined in plants, Xuelu will have the unique opportunity to make a large contribution to signaling mechanisms that control plant growth.

BRI1 is a member of the largest class of receptor kinases in plants. Plant genomes contain more than 400 receptor serine/threonine kinases, yet a mechanism of activation for any of them is unknown. Of these 400 receptors, the largest class comprises over 200 members that contain leucine-rich-repeat s in their extracellular domains. The ligand and signaling pathway is known for just a few of these LRR-kinases, one of which is the steroid receptor, BRI1. Xuelu has utilized the BRI1 receptor and signaling pathway as a springboard to begin to determine a mechanism for activation of the plant receptor kinases. Using a combination of biochemistry and genetics, his results support a model whereby BRI1 activation involves a series of steps which involves a ligand-induced conformational change through a preformed homo-oligomer, followed by the transphosphorylation of the kinase domain to release the autoinhibitory influence of the C-terminus, which then allows further phosphorylation of BRI1 to fully activate the receptor. The major divergence of his model from that of the well-studied TGF β receptor S/T kinase is that the kinase domain of T β RII is constitutively phosphorylated in a ligand-independent manner, and ligand binding to both T β RII and T β RI primarily induces the proximity and phosphorylation of T β RI. In contrast, Xuelu's data suggest that BRI1 kinase cannot be efficiently phosphorylated and activated without BL-binding. As such, Xuelu's studies are of interest to scientists studying signaling both in plant and animal systems. His results were published earlier this year in *Developmental Cell*, and constitute a very substantial contribution to the plant signaling literature.

Very few studies have approached this level of analysis for any signal transduction component in a plant system. I respect Xuelu's tenacity and dedication to do in vivo kinase assays and map phosphorylation sites in BRI1, as well as to map the functions of various

domains of BRI1. He has become an expert biochemist and knows the animal receptor kinase literature in great depth. Xuelu has taken the initiative to seek the sage advice of Tony Hunter and his long-term technician, Jill Meisenhelder, who have guided him in his experimental design. I am impressed by his resourcefulness and his desire to get the answer.

Xuelu has also undertaken a project to look for in vivo substrates of BRI1's kinase, and has identified several good candidates. One of them looks particularly interesting in that its phosphorylation by BRI1 leads to its dissociation from the membrane. He is currently doing the follow-up biochemistry and reverse genetics to better define the role of these proteins in the BRI1 signaling pathway. These studies should also lead to one or two significant papers, which he will write later this year.

The combination of projects that Xuelu has chosen has allowed him to gain expertise in plant genetics, molecular and cell biology, and biochemistry. He has combined his previous experience in maize genetics and development with molecular and biochemical techniques that he has learned since arriving in my lab. I am delighted to have him here and view him as a valued colleague. I am confident that Xuelu will continue to make important contributions to the brassinosteroid project while in my lab. He also has my complete endorsement to continue these studies in his own laboratory.

Xuelu will also be an excellent colleague and teacher. Xuelu works well with technicians and undergraduate students, taking the time to mentor them, as well as getting them to work productively. He makes valuable and thoughtful suggestions at our lab's group meetings. Thus, I anticipate that he will run an effective lab, as well as interact well with undergraduate and graduate students.

In summary, Xuelu Wang combines the right qualities of scientific breadth and depth to be a successful academic scientist. He would be an excellent choice for faculty positions in molecular genetics, cell biology, or biochemistry. I think that you will find him to be an interactive colleague, and I recommend him to you with enthusiasm. If you have any other questions, please feel free to contact me.

Sincerely and best wishes,



Joanne Chory
Professor, The Salk Institute
Director, Plant Biology Laboratory
Investigator, HHMI