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

Re: **Yiwei Jiang**

It is truly a pleasure to write a letter of recommendation for Yiwei Jiang in support for his application for a position in your department. Yiwei is one of the *best* graduate student I have seen during my nineteen years at the University of Utah, and he compares favorably with the *best* post-docs I worked with at the MRC Laboratory of Molecular Biology.

Yiwei cloned the *SIN4* gene as a rotation student, and then after he joined my lab he sequenced and characterized the gene by constructing gene disruptions, determining localization by immunofluorescence, etc. Yiwei demonstrated that *SIN4* has unusual properties as a transcriptional regulator, reducing expression of some genes and derepressing others. He showed that *sin4* mutants have several phenotypes in common with histone mutants, leading to the suggestion that *SIN4* is involved in chromatin structure. Yiwei then demonstrated that *SIN4* and *RGR1*, another pleiotropic transcriptional regulator, both regulate the same genes, and that Sin4 and Rgr1 proteins co-precipitate. *SIN4* is required for full expression of *HIS4*, a gene where the chromatin structure of the promoter is believed to be important. Yiwei constructed a variety of isogenic strains with multiple mutations in regulators of *HIS4*, and showed that the *sin4* mutation has a similar effect on *HIS4* regulation as a promoter mutation in the Rap1 binding site, consistent with a *SIN4* effect via chromatin.

Yiwei demonstrated that a *sin4* mutation has an Spt- phenotype, and he then showed that only a small fraction of *sin4* cells with a *his4-912 $\delta$*  promoter are His+. These results suggest that Spt suppression is epigenetic. To test this, Yiwei constructed strains with an "Spt" promoter driving *ADE2* expression, where stable inheritance of "on" and "off" states can be monitored by colony color sectoring assays. None of the mutants produced a variegated colony phenotype, as they were either fully white or fully red. Yiwei then initiated a screen for mutations that would allow a strain with this *his4-912 $\delta$ :ADE2* reporter to sector. He has focused on one complementation group of mutants, and he determined that mutations in an essential actin related protein produces the phenotype. In an important set of experiments Yiwei showed that this epigenetic effects are controlled at the transcriptional level. This is an exceptional study, and Yiwei deserves all the credit.

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In collaboration with Roger Kornberg's lab, Yiwei showed that the Sin4 protein is part of the RNA polymerase II holoenzyme/mediator complex, and he then decided to pursue postdoctoral studies on transcriptional regulation in Roger Kornberg's lab. I think this was an excellent choice, for he has now learned biochemistry from a master. Yiwei is now in a position to use both genetics and biochemistry in studies in his own lab. Importantly, Yiwei is not afraid to take on new or difficult methods, if it is the right method for the job at hand.

Let me tell one story. As an example, Yiwei hypothesized that the effects of the *sin4* mutation could be via chromatin. He read in one of the Grunstein lab's histone depletion papers where chloroquine gels could be used to detect nucleosome loss from circular DNAs. He read up on the method, did the experiment, and got it to work the first time. Had he asked me first, I probably would have advised against this experiment because I had seen postdocs at the MRC struggle with the method. After we published our results with the chloroquine gels, I have talked with several labs that suffered through many technical problems or were asking us for advice.

Yiwei is a gifted scientist who is becoming an outstanding independent investigator. In addition to being bright, hard-working, and industrious, he is very creative in the lab. Moreover, Yiwei is a critical thinker. In lab meetings or journal clubs while at Utah, Yiwei did not ask a lot of questions; however, when Yiwei did ask a question or offer a suggestion, everyone listens carefully. Yiwei's comments reveal real insight and analytical thought. I should point out that while in my lab, it was Yiwei's reading the literature and synthesizing information, not mine, that led to the idea that *SIN4* is involved in chromatin structure.

Clearly, Yiwei is extraordinarily productive. Yiwei was a real pleasure to have in my lab, and he will be a valued colleague. Although not very gregarious, Yiwei gets along well, and his advice is eagerly sought by others. Yiwei has an excellent command of the English language, a good vocabulary, and he is a good speaker. Yiwei took an English writing class (Technical Writing for Non-Native Speakers) while at Utah, and he has a good understanding of English grammar and tenses, often a problem for Chinese students. His strong writing skills are evident from his record of publications and grants since starting his own lab.

The work that Yiwei is doing currently on co-suppression of the Ty1 retrotransposon is some of the most novel and innovative that I have seen years. It is an exciting system, and I am certain that many good things will come of it. It is unfortunate the situation in his current department has deteriorated to this point. However, this may be to your benefit!

In summary, Yiwei is truly exceptional. When he was in my lab he was always able to keep multiple projects up and running at the same time, and it appears that he has upped the pace since starting his own lab. I give him my highest recommendation. You will not be disappointed. If you have any questions, please contact me.

Sincerely,

David Stillman  
Professor



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**CONFIDENTIAL**

September 20, 2005

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Dear Committee Members:

I am writing in regard to the candidacy of **Yi Wei Jiang** for a faculty position in your institution. I have known Jiang since the middle of his graduate career when we collaborated in research on the yeast Mediator of transcriptional regulation. Together we established that Mediator, originally identified on the basis of its requirement for transcriptional activation, plays a key role in repression as well. I was greatly impressed by Jiang's insight, precision, and alacrity during the course of that work.

Joining my laboratory as a postdoctoral fellow, Jiang took up the challenge of transcription control in higher organisms. The prevailing view at the time was that enhancer-promoter communication in higher cells could be attributed to the TAF complex, and that Mediator was possibly unique to yeast. Jiang succeeded in isolating a multiprotein complex from mouse cells containing several homologs of yeast Mediator subunits. He went on, with additional members of our group, to establish the physical and functional similarity of yeast and mammalian Mediator complexes. His work, together with that done at the same time or soon after in other laboratories, indicates that Mediator rather than TAFs provides the interface between regulatory proteins and the transcription apparatus.

Jiang is very smart, vigorous, and effective. He exhibits an unusual command of theory, facts, and technical material. Although a geneticist by training and inclination, he has shown a capacity for biochemical fractionation and manipulations as well. He therefore possesses all the tools for a productive career in bioscience. What really sets him apart from most others, however, is his independence of mind and longstanding pursuit of his own research problem. He discovered a fascinating type of epigenetic control of transcription while a graduate student, through astute observation and penetrating experimental analysis. This work was evidently instigated by him, and the experiments were of his own devising. He continued this same line as a postdoc, in parallel with his pursuit of mammalian Mediator, broadening the concept of epigenetic control and extending the factual support. Again the work was entirely independent, and it provided a basis for the formation of his own laboratory. He has gone on to do work of comparable originality, with which I am less familiar, but which I believe attests to his capacity for leadership as well as individual research accomplishment.

Sincerely,

Roger Kornberg,  
Professor

RDK:jjl