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November 27, 2005

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

Dr. Brun;

This letter is written in support of Jiajian Liu (JJ), who is seeking a Systems Biology/Microbiology faculty position in your department. JJ was a graduate student in my lab from 1995-2000 in the Department of Biochemistry and Molecular Biology at LSUMC-S, Shreveport and later at Oregon Graduate Institute of Science and Technology, Department of Biochemistry and Molecular Biology. He received his Ph.D. from LSU.

As a rotation student in my lab, JJ examined the relationship between the regulation of motility and the cell-density dependent control of competence development in *Bacillus subtilis*. Motility genes, such as *hag* that encodes the major flagellar protein, flagellin, require the sigma D form of RNA polymerase for their transcription. The transcriptional activation of the competence regulon requires the ComK protein, which directly stimulates transcription initiation at late competence operons, the products of which function in DNA uptake. JJ found that the late competence operon, *comF*, which is transcriptionally activated by ComK, is fused to the operon that contains *flgM*, encoding the sigma D anti-sigma factor. He demonstrated that *flgM* operon transcription is stimulated through the cell-density dependent activation of ComK. We proposed that the transcriptional activation of the *comF-flgM* operon results in down-regulation of motility functions in response to high cell density. This work appeared in a Journal of Bacteriology publication on which JJ was first author. The ComK-dependent activation of *flgM* expression was confirmed by work performed in the laboratory of D. Dubnau (Mol Microbiol. 2002, 43:1331).

JJ next undertook a project to determine the factors influencing the activity of the sigma H form of RNA polymerase, which is necessary of the transcriptional activation of many genes that function in developmental processes of *B. subtilis* including sporulation and competence development. He, along with a postdoc, Dr. Mark Cosby, showed that Sigma H is subject to post- translational regulation involving proteases LonAB and ClpX. While evidence was uncovered showing that Lon affected Sigma H turnover, ClpX was required for another function in the activation of the Sigma H form of RNA polymerase in cells of stationary phase cultures. This work was published in Molecular Microbiology as a full-length paper on which JJ was first author. JJ, in collaboration with Dr. Michiko Nakano, isolated suppressors of *clpX* mutation that restored sigma H-dependent transcription, as well as other pleiotropic effects, and these mapped

in the *rpoA* gene in the region encoding the alpha C-terminal domain. His contribution appeared in a Molecular Microbiology paper in which he was a co-author. JJ has constructed an intein based expression system for production of *B. subtilis* ClpX and has also purified *B. subtilis* RNA polymerase from wild type and *clpX* mutant cells to examine holoenzyme composition and the effect of ClpX on the activity of Sigma H holoenzyme. In his third first author publication in Molecular Microbiology, he showed that ClpX preferentially stimulates σ^H-dependent transcription in vitro. We now know that ClpX stimulates transcription by interacting with the RNA polymerase-binding protein, Spx (Nakano et al. 2003. Proc. Natl. Acad. Sci. 100:4233), which co-purifies with RNA polymerase (unpublished).

After earning his Ph.D., JJ chose to expand his research experience by joining the G. Stormo group for postdoctoral training in computational biology. This has been a successful endeavor as he will have published at least three significant publications by the time his postdoctoral work is completed. Of particular significance is his work that has uncovered a DNA-binding code of Zn-finger proteins.

I have never had a more hard-working graduate student than JJ. He was quite productive, both in terms of his bench work and his efforts to understand the considerable body of literature that deals with prokaryotic transcriptional regulation. What impressed me most was JJ's willingness to tackle new and difficult experiments involving unfamiliar technology in order to to answer crucial questions pertaining to his project. His efforts in understanding the literature along with his accumulated experience in both genetics and biochemistry resulted in an enhanced ability to design controlled, meaningful experiments and fostered innovation and independence on his part. JJ also worked hard at improving his presentation skills in weekly lab meetings and contributed significantly in the preparation of his manuscripts.

I highly recommended JJ in the strongest terms. Please contact me at 503-748-7335 if you require more information.

Sincerely

Peter Zuber, Professor