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Yves Brun, Ph.D.
Systems Biology/Microbiology Faculty Search
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Jordan Hall 142, 1001 E 3rd Street
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September 19, 2005

Dear Prof. Brun,

It is with great pleasure that I write a letter of recommendation on behalf of Dr. Mike Axtell. I have known Mike since August 1998 when he completed a rotation research project in my lab in the Department of Plant and Microbial Biology at the University of California, Berkeley. As a collaborator and member of his thesis committee I was in close contact with Mike throughout his graduate career. He is unquestionably one of the best graduate students that I have met since joining UC Berkeley in 1987. I would rate him among the top 1% of all students in biological research at UC Berkeley with respect to scholarship, ability and potential for success in a research and academic career. He is highly intelligent, hard working and exceedingly productive, and I am absolutely certain that he will continue to be a highly successful and outstanding academic researcher.

Mike's outstanding research skills were evident in his ten weeks as a rotation student in my lab. He completed his project successfully and answered an important question regarding the nature of the tobacco mosaic virus protei recognized by the plant resistance protein, N, which is a member of the Toll-Interleukin-1 receptor-like (TIR) family. Mike is a co-author on a manuscript from my group describing the biochemical properties of the TMV elicitor protein. Mike also collaborated with a postdoctoral colleague in my lab on a project to determine the role of a MAP kinase kinase kinase (MAPKKK) homolog of human MEKK1, NPK1, in pathogen-resistance pathways. Mike is a co-author on the manuscript describing this work recently published in *Developmental Cell*.

Mike's graduate research in Brian Staskawicz's lab addressed one of the major and most challenging problems in the field of plant innate immunity: the mechanism of host recognition of pathogen "avirulence" proteins. Mike's findings are among the most exciting in the field and constitute a major leap in our understanding of the mechanism of plant innate immunity. In particular, his work has provided numerous key insights into the recognition of pathogens via R proteins and cellular proteins. His results provide strong support for the "guard hypothesis" and show that the R protein, RPS2, and RIN4, a

cellular protein targeted by the pathogen avirulence protein AvrRpt2, are physically associated in planta prior to infection. Through an elegant set of experiments, Mike showed that AvrRpt2 introduction into the cell leads to elimination of RIN4, implying that RPS2 recognition of AvrRpt2-delivering pathogens may be the result not of a direct molecular interaction between RPS2 and AvrRpt2, but of the elimination of the RPS2-bound RIN4 protein.

Mike's graduate work resulted in two first-authored and two co-authored manuscripts. I have kept in contact with Mike since he graduated. His work as a post-doctoral fellow at the Whitehead Institute has also yielded interesting results. I am very impressed with the paper he recently published on the antiquity of microRNAs and their targets in land plants. His future plans to explore the role of small RNAs in development are most promising. I attribute Mike's significant research progress to his scholarship and willingness to develop or employ any method that best addresses the problem.

Mike has proven himself to be an excellent and willing teacher, with in-depth knowledge of the field of plant disease resistance and the broader biological sciences. His seminars are organized, flawlessly presented and very informative. Mike is also a superb writer. It has been a pleasure to read his graduate exam proposals, thesis, and manuscripts.

Mike's intelligence and productivity in his research endeavors are matched by his kindness, even-temper and fine sense of humor. As a graduate student, Mike's interactions with his colleagues were exemplary. He established an exceptionally good rapport with all colleagues and was frequently sought out for advice and materials. Mike is greatly appreciated by the members of the Plant and Microbial Biology Department and by leaders in the plant disease resistance field around the world.

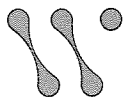
In summary, Mike is unquestionably among the best researchers I have encountered. In my 30 years in the field, I have come across very few scientists who exhibit his level of intellectual depth and scientific distinction. Mike is truly talented and I am certain of his future success as a researcher and academic. Please do not hesitate to contact me with any questions.

Sincerely,

A handwritten signature in black ink, appearing to read 'Barbara Baker', with a stylized, flowing script.

Barbara Baker
Adjunct Professor
Plant Gene Expression Center
Department of Plant and Microbial Biology
University of California, Berkeley

WHITEHEAD INSTITUTE



September 26, 2005

Yves Brun
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David Bartel, Ph.D.
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Dear Dr. Brun,

I am writing to enthusiastically recommend Michael Axtell for the junior faculty position in your department. Mike has been a postdoc in my lab for the past two years.

Before coming to my lab Mike was already recognized as one of the top young scientists in plant biology, having carried out an excellent Ph.D. dissertation with Brian Staskawicz (UC Berkeley), where he made major contributions to the understanding of how the plant innate immune system can recognize assaults from such a wide variety of different pathogens. Based on this work and his research proposed for my lab, Mike was awarded a Helen Hay Whitney Postdoctoral Fellowship.

My lab studies microRNAs. MicroRNAs are small, endogenous regulatory RNAs that can direct the repression of protein-coding genes. Much of our work is in animals, but in 2002, collaborating with a plant geneticist, we found microRNAs and their regulatory targets in *Arabidopsis*. Since then, Mike and two other accomplished plant biologists have joined the lab, and together with some students we have explored in much more detail the genomics and regulatory functions of these tiny RNAs. As I expected, Mike has been a leader in this effort, carrying out an impressive series of experiments, and also playing a key role in advising two graduate students on the methods and biology of *Arabidopsis*.

Mike started off investing considerable effort in developing sensor technology for examining where microRNAs are expressed. However, when he noticed that reporters sensitive to microRNA regulation have a striking propensity to be globally silenced, he decided to shift his focus to developing a microarray for microRNA detection. When he profiled basal plants he discovered that many of them were conserved beyond flowering plants—some all the way down to mosses. Mike then developed the first molecular method to find the transcripts targeted by the microRNAs and applied it to find the targets of some of the deeply conserved microRNAs. His method was crucial because the genomes for these species were not sequenced, and the ESTs coverage was far from complete, rendering our computational methods ineffective. Remarkably, each of the targets Mike found was orthologous to previously confirmed *Arabidopsis* targets, suggesting that these microRNA-mRNA regulatory modules have been intact throughout the

evolution and diversification of land plants. We published these results last summer (Axtell & Bartel, *Plant Cell* 17:1658-73) in a paper that was selected for a Research Highlight in the 26 May issue of *Nature*.

In work that Mike will be submitting this fall, he has found not only the conserved but also the non-conserved silencing RNAs in moss and lycopods. He has now discovered as many microRNAs in moss as had previously been found in flowering plants. He also has some very interesting results regarding other silencing RNAs (including trans-acting siRNAs) in the basal plants. This study will establish Mike as the world's authority on RNA silencing in basal plants and will constitute an impressive foundation for future studies in his own lab.

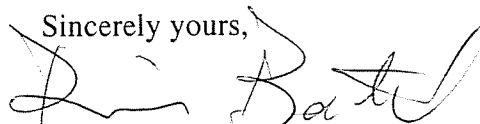
I am very impressed with Mike and what he has accomplished in a short time in my lab. Mike is always at the forefront of new technologies. I mentioned the pioneering work he has done with microRNA expression arrays and target identification. He was also the first in the lab to confirm targets experimentally—bringing that technology to the lab has been crucial for others working in both plants and animals. Last month he led the lab in adapting our cloning protocol to be suitable for high-throughput sequencing, and so we are now eagerly awaiting the arrival of more than a million reads of lycopod and moss small RNAs. I am sure he will continue to be an innovator and early adaptor of new technology and that this will serve him well as he establishes in his own lab. For example, he has already done some pilot gene knockouts in moss, demonstrating the feasibility of his research plan.

In addition to the molecular work, Mike has recently taught himself Perl programming so that he can automate the analyses of the several thousand reads that he has in hand (and the million or so that will be arriving soon). This newly acquired expertise with computation, just another example of his desire do what it takes to answer the most interesting biological questions, will position him well for the biology of the future.

Mike is an excellent communicator. His seminars and writing are clear, interesting and informative. I am certain he will be a great teacher.

In summary, Mike is a world expert on the genomics, functions, and evolution of microRNAs. He would be a great addition to any department wanting to instantly strengthen their presence in the RNA silencing field or wanting to bridge ties between computational and experimental science. He has everything it takes to succeed as an assistant professor and beyond—the type of young scientist we try to recruit for faculty positions here at MIT. I'm sure you will also find him to be a friendly, interactive, and trustworthy colleague. I recommend him to you most highly and without reservation.

Sincerely yours,



David Bartel, Ph.D.

Member, Whitehead Institute

Professor of Biology, MIT

Investigator, HHMI

27 September 2005

Prof. Yves Brun
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Dear Yves,

Michael Axtell

I am pleased to write in support of Michael Axtell's application for a faculty post in your department. I met Michael initially through his time in the Staskawicz Laboratory, with which we have good links. Subsequently I have maintained contact with him through his published work both there and in the Bartel group and at conferences.

My impression of Michael is that he is a first rate scientist with an excellent future. He has a broad background – taxonomy, defense, RNA regulation – that he uses fully in his work. The recent ancient miRNA paper is an example of his ability to use diverse approaches – there is technology development, computing and evolutionary thinking. Michael's earlier paper on RPS2-specified disease resistance is, in my opinion, a landmark paper in the disease resistance field. The clarity of writing and experimentation make it stand out from some of the other papers including those on similar topics. I am sure that it will continue to be cited for some time to come.

In addition to his academic qualities, Michael has the personal characteristics of a successful research group leader: he is approachable and easy going but not afraid to participate fully in discussions.

I have been interested in Michael's work because he spans the two fields – RNA silencing and disease resistance – that are primary interests in my own laboratory. He is precisely the type of individual that I would like to attract here and I was disappointed that he did not even want to apply for our vacant positions – for geographic reasons he said. You will be fortunate to attract him to Indiana and I wish you luck!

Yours sincerely

Professor David Baulcombe FRS
Senior Research Scientist



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September 25, 2005

Yves Brun
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Dear Dr. Brun,

The following letter is in support of Mike Axtell's application for an Assistant Professor in your Department. Mike is without question the best graduate student I have had during my twenty two years at UC Berkeley. He is extraordinarily bright, hard working, and extremely productive. Mike is an excellent experimentalist and is able to definitively design and effectively carry out complex experiments. He reads widely on many subjects in biology and as a result has a strong grasp of the literature in many different fields. In addition, Mike is a gifted writer which will serve him well as a faculty member.

Mike's work in my lab involved the elucidation of the mechanistic basis of recognition and specificity in *Arabidopsis* innate immunity. The work that Mike carried out in my lab led to a major advance in our understanding of how the bacterial effector protein AvrRpt2 induced the RPS2 disease resistance. His work demonstrated that the bacterial Type III effector protein, AvrRpt2, is a cysteine protease that eliminates a host protein called RIN4. The elimination of this protein is directly coupled to the activation of the Rps2 disease resistance pathway.

Mike is also a pleasant individual and a good lab citizen as he gets along with everyone in the lab. I have always been impressed with the passion and rigor that Mike approaches his work. He is undaunted to tackle any task and he has a great talent to design and definitively test his hypotheses in the most straightforward ways. As a potential faculty member, I have no doubt that Mike will become a leading force in the area of plant micro RNAs and will make many significant contributions in the future. Thus, I enthusiastically recommend that Mike be seriously considered by your committee for this position. I do not usually give such a strong letter of recommendation but in this case it is justified. He is superb! If I can be of any further assistance please do not hesitate to contact me.

Brian Staskawicz
Maxine J. Elliot Professor and Chair of Plant and Microbial Biology