CALIFORNIA INSTITUTE OF TECHNOLOGY

Pasadena, California 91125

Elliot M. Meyerowitz
George W. Beadle Professor of Biology
Chair, Division of Biology

meyerow@caltech.edu
(626) 395-6889
FAX (626) 449-0756

October 11, 2005

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

Dear Dr. Brun:

I write to strongly recommend Frank Wellmer for a faculty position. Frank has been a postdoctoral scholar and senior postdoctoral fellow (a research faculty position) in my laboratory since September, 1999 – six years. In that time he has pioneered the transcriptional profiling of developing flowers, leading to several important discoveries, with the promise of many more.

Frank came to my lab after a Ph.D. in the lab of Eberhard Schäfer at the University of Freiburg in Germany. In Schäfer's lab he worked on the biochemical characterization of basic leucine zipper transcription factors in plants (in particular in parsley). He had earlier completed a Master's degree at the University of Osnabrück, working with Wolfgang Junge on mutants of chloroplast ATP synthases. He came to my lab with remarkable recommendations. Schäfer wrote "Frank belongs to the top 3 of the ca. 30 grad students, which have ever worked in my lab over the last 25 years, at the end of the work he even may have been the very top scientist..." Among the adjectives Schäfer used to describe Wellmer are "clearly outstanding", "fascinating, communicative", and "excellent." His other letters were as good - Junge, wrote that he is a "skillful and energetic worker, equally enthusiastic and critical about his experiments...Because of his dedication, self-determination, skills and work capacity, I don't hesitate to recommend him..." Prof. Dr. Gunther Neuhaus of Freiburg wrote that he will be an "excellent member of any lab, scientifically and socially."

All of this has turned out to be true. When Frank arrived in my lab, microarray analysis of RNA profiles was in its infancy, at least in plants. He drove our effort to tame this technology, first by making (with some others in the lab) cDNA microarrays, and then when they were available, arrays made with spotted oligonucleotides representing all of the annotated genes of Arabidopsis. Our decision to make our own arrays was based on cost and sensitivity – the types of experiments Frank and others here planned required

sensitive detection of RNAs from a large number of genotypes, developmental stages, and time points after gene induction – by now he and the others here have probably hybridized 1,000 arrays. Spotting our own was the only way we could do so many experiments. Frank and José Luis Riechmann worked out the entire technology, to the point where we now have extremely robust and high-quality arrays of great sensitivity. Frank not only understands and does every step in producing such results, but has also become expert in the use of the analysis software (we rely mainly on Rosetta Resolver, but Frank's expertise goes beyond just one suite of programs).

This is not all of course, and I mention the technical aspects to make it clear that Frank will not have to rely on others to continue his experiments – he has expertise in the methods, and could establish them in his own lab. The interesting part is what he has done with the arrays. I'm sure he will describe this to you; in brief he used the cDNA and oligonucleotides arrays to establish a time course of RNA accumulation in developing flowers – first with a system whereby flowers are simultaneously induced in callus tissue to give sufficient early flowers for a degree of analysis (Wagner, D., Wellmer, F., Dilks, K., William, D., Smith, M.R., Kumar, P.P., Riechmann, J.L., Greenland, A.J. and Meyerowitz, E.M. (2004) Floral Induction in Tissue Culture: a System for the Analysis of LEAFY-Dependent Gene Regulation. Plant J. **39**, 273-282), and then with an even better system of his own invention described below. While this database of temporally regulated floral development genes was being created, he also did array comparisons of later-stage flowers of different homeotic mutant genotypes. These comparisons provided a database of the spatial expression patterns of RNAs in flowers – which RNAs are specific to individual floral organs, and which are not (Wellmer, F., Riechmann, J.L., Alves-Ferreira, M. and Meyerowitz, E.M. (2004) Genome-Wide Analysis of Spatial Gene Expression in Arabidopsis Flowers. Plant Cell **16,** 1314-1326). So now we know where and when thousands of RNAs are specifically expressed during flower development.

Frank then set up several systems for temporal analysis of the genes activated after induction of individual floral organ identity (homeotic) genes, to answer in part the long-standing biological question of how homeotic regulatory genes lead to segmental or organotypic differentiation. Along with another postdoc here, Toshiro Ito, he followed the time course of RNAs activated and repressed after induction of the *AGAMOUS* gene, which specifies stamen and carpel development. Among the downstream genes discovered was *NOZZLE*, also known as *SPOROCYTELESS*. Frank and Toshiro showed that this gene is directly activated by *AGAMOUS* and that it is sufficient to induce microsporogenesis in floral organs – showing how, step by step, homeotic genes lead to specific cell types (Ito, T., Wellmer, F., Yu, H., Das, P., Ito, N., Alves-Ferreira, M., Riechmann, J.L. and Meyerowitz, E.M. (2004) The Arabidopsis homeotic selector protein AGAMOUS directly controls a gene involved in microsporogenesis. Nature **430**, 356-360). Along with another postdoc, Hao Yu, Frank studied genes repressed by activation of floral induction genes, thereby finding a new class of floral regulatory gene that promotes shoot identity, and that must be repressed for floral meristems to develop to flowers (Yu, H., Ito, T., Wellmer, F. and Meyerowitz, E.M. (2004) Repression of *AGAMOUS-LIKE 24* promotes floral meristem identity in flower development. Nature

Genetics **36**, 157-161). With a graduate student, Catherine Baker, and another postdoc, Patrick Sieber, he analyzed the control of members of the NAC family of transcription factors in developing flowers, findong that the control in early flowers is in part by the stage- and cell-type specific action of a family of microRNAs (Baker, C.B., Sieber, P., Wellmer, F., and E.M. Meyerowitz (2005) The *early extra petals1* mutant uncovers a role for microRNA *miR164c* in regulating petal number in *Arabidopsis*. Curr. Biol. **15**, 303-315).

Following this work, Frank took on early flower development in vivo, not in culture, and developed new methods that allowed a much more thorough analysis than previously. The problem with analysis of gene expression in early flowers has been that they are tiny, an the nature of the *Arabidopsis* inflorescence is such (racemose) that flowers initiate sequentially, so that only one flower of any developmental stage is present on a single inflorescence stem. Previous experiments purporting to report RNAs expressed in early flower development either were based on RNAs from mixtures of flowers of different stages, with the earliest flowers so small compared to later ones that their RNAs were perhaps not detected; or were from flowers in culture (our own earlier experiments), which do not in some respects reflect what happens in a growing plant. Frank solved this problem by setting up a novel genotype (p35S::AP1-GR; *ap1*; *cal*) in which inflorescences are converted to a cauliflower morphology (large numbers of meristems halted at the same stage of development), and then induced to make large numbers of normal flowers simultaneously by addition of a small-molecular activator (dexamethasone). Using this system he did a detailed analysis of RNA repression and induction in early flower development, which has resulted in new information and new conclusions, as well as in a manuscript that we have just submitted to Nature Genetics (Wellmer, F., Alves-Ferreira, M., Dubois, A., Riechmann, J.L. and Meyerowitz, E.M. (2005) Genome-Wide Analysis of Gene Expression during Early *Arabidopsis* Flower Development, submitted for publication)

Frank is now engaged in even more experiments, following genes activated downstream of *APETALA1* in early flowers, and following up on the hundreds of regulatory genes that he is now fitting into an analysis of the gene circuitry that leads to flowers. He clearly has a bright future in plant developmental genetics, and is superbly trained in plant biochemistry, genetics, development, and genomics. He works extremely hard, is clearly productive, is innovative both at the level of techniques and of experimental strategy, and he works marvelously with others, as indicated by the collaborations he has in my lab. I expect he would be a first-rate lab leader, and that he will continue to be a major contributor to our understanding of the genetic basis of development in plants.

Sincerely,

Elliot Meyerowitz

Lehrstuhl für Botanik, Institut für Biologie II, Schänzlestr. 1 • D-79104 Freiburg

Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 E 3rd St

USA - Bloomington IN 47405-7005

ALBERT-LUDWIGS-
UNIVERSITÄT FREIBURG
Lehrstuhl für Botanik
Institut für Biologie II
Prof. Dr. E. Schäfer
Schänzlestr. 1
79104 Freiburg
Telefon 0761/203-2683
Telefax 0761/203-2629
e-mail:
Eberhard.Schaefer@biologie.uni-freiburg.de
http://www.biologie.uni-freiburg.de

Aktenzeichen:
Bearbeitet von: B. Eiter
Telefon-Durchwahl: 0761/203-2658
Datum: 12. Oktober 2005

Letter of recommendation for Dr. Frank Wellmer

It is a pleasure for me to write a letter of recommendation for Dr. Frank Wellmer because I know him as an outstanding graduate student in my laboratory and have followed his research in Elliot Meyerowitz' laboratory carefully.

Frank applied to a graduate programme at Freiburg and chose my lab to work on the light regulation of the CPRF transcription factor family from parsley. He performed a very independent PhD thesis with an exceptional outcome. His biochemical expertise and his engagement in science – the top I have ever observed from a graduate student in more than 30 years – led to a series of high-profile papers describing the light-dependent regulation of two CPRF transcription factors. His work was selected as that year's best PhD thesis at our department and he was awarded the prestigious Emmy Noether fellowship to work in Elliot's lab on a totally different subject. So not only from his master to his PhD thesis but also for his post doc he changed fields completely, is atypical for German scientists. Due to the establishment of new techniques in Elliot's lab there is a 3-year-gap in his publication record. But as indicated by his publications in 2004/ 2005 and the vast amount of unpublished results – partially described in his proposal – this big investment turned out to be highly beneficial.

Clearly, he can use this material to build up a creative and productive new research group and I do not have the slightest doubts that he will be extremely successful in doing so. This judgement is based on his personality structure and the

scientific productivity he has already shown. His proposed research project is innovative and straight-forward at the same time. It addresses in very elegant ways the questions that should be answered to understand the regulatory networks controlling differentiation processes and development. This step is essential for identifying the hierarchical orders in a complex signalling network and represents, at least in my opinion, the best approach to obtain the necessary data for a systems biology approach.

Therefore, I strongly recommend Frank for a faculty position and think every university can and will be glad to have him as a faculty member.

Finally, a few comments about his teaching engagement and his social skills. Here, I can only judge his time as a graduate student. He was really excellent in supervising undergraduates working in my laboratory, stimulated discussions and guided them to become independent. As a teaching assistant, he was equally engaged in promoting the top of the class and helping the less talented to increase their knowledge.

During the graduate programme he organized not only PhD student meetings and weekend programmes but has also been a driving force to organize a scientific meeting. Both, his interactions within the group, with visiting scientists and outside collaborations were excellent. He is one of the few persons of whom I can say it is a great pleasure to have him around either within a group of in a department. He will always strongly interact with others and both sides will have great benefit.

Therefore, I am also strongly convinced that he will be an excellent teacher in your programme.

Yours sincerely,

Prof. Dr. E. Schaefer

ZMBP

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

ZENTRUM FÜR MOLEKULARBIOLOGIE DER PFLANZEN

ZMBP · Auf der Morgenstelle 1 · D-72076 Tübingen

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

Prof. Dr. Klaus Harter
Pflanzenphysiologie

Telefon: +49-(0)7071-29-72605
Telefax: +49-(0)7071-29-3287
E-Mail: klaus.harter@zmbp.uni-tuebingen.de
http://www.uni-tuebingen.de/ZMBP

07.10.2005

Letter of reference for Frank Wellmer, Ph.D.

Dear Dr. Brun,

In support his application at Indiana University, Dr. Frank Wellmer has asked me for a letter of reference.

I am a full professor at the Plant Physiology Department of the University of Tuebingen, Germany, performing research on Plant Molecular Physiology and Developmental Biology. I am considered an expert in the field of plant signal perception and signal transduction.
As I was Frank Wellmer´s supervisor during his Ph.D. at the University of Freiburg, Germany, I know him personally very well and can therefore judge a major part of his work and his personality.

During his Ph.D. Frank concentrated on the regulation of the intracellular distribution and of the activity of bZIP transcription factors from parsley. During that time he developed outstanding biochemical talents and contributed extraordinarily to the biochemical knowledge of the laboratory in Freiburg. In his work Frank demonstrated that the bZIP factors CPRF1, CPRF2 and CPRF4a, though very homologous, were regulated quite differentially on the posttranslational level in parsley and carried out surprisingly different functions. Furthermore, he was involved in the development of immunolocalization techniques for the detection of low-expressed bZIP factors in plant cells. His data encouraged me to continue the analysis of plant bZIP factors in even more detail and to extend our research to Arabidopsis and other plant species.

Four papers, which were published in high-impact journals as for instance *J. Biol. Chem.* and *J. Cell Biol.*, derived from Frank Wellmer´s thesis.

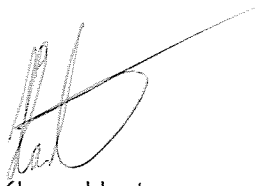
I would also like to mention that during his Ph.D. Frank never needed major supervision, because he developed most of the scientific ideas by himself and carried out the experimental approaches almost independently.

During his postdoc in the laboratory of Dr. Elliot Meyerowitz, Frank extended and deepened his knowledge of plant molecular biology and used the genechip technique to unravel the spatial and temporal expression of flowering-related genes (see his recent publications). In his future research Frank Wellmer intends to concentrate on the functional analysis of novel regulatory genes acting downstream of the key floral regulators. Because he is able to combine biochemical and cell biological tools with state-of-the-art molecular approaches (microarray, ChIP), I am absolutely sure that he will in future continue to contribute very successfully to the research on floral development in higher plants.

From my personal experience, Frank Wellmer is a very open-minded, easy-going, helpful and exceptionally talented person, very well suited to perform excellent academic research and to lead a science team. During his time at the University of Freiburg, he also gained experience in teaching undergraduate and graduate students. Frank Wellmer works with great commitment and enthusiasm on the complicated areas of plant transcription factors and floral development.
I also know that he is always very interested in scientific topics not directly dealing with his own field and is able to get into new and complicated topics of research surprisingly fast.

In conclusion, I would like to point out that, due to his personality and excellent research talent, Frank is very well suited for the position he has applied for.
Thus, I strongly support Dr. Frank Wellmer´s application.

Yours sincerely,



Klaus Harter