

HARVARD MEDICAL SCHOOL  
DEPARTMENT OF BIOLOGICAL CHEMISTRY  
AND MOLECULAR PHARMACOLOGY

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October 7, 2005

Letter of recommendation for **Miriam Bucheli**

I know Miriam Bucheli because she works in the lab of Steve Buratowski, a colleague in my department who works on related scientific issues and with whom we have joint laboratory meetings. In addition, I accepted Miriam as a postdoctoral fellow in my laboratory, although she ultimately chose to work with Steve, in large part because her interests fit better. I have heard Miriam talk about her work in our joint group meetings, and I have had several discussions about her work and other career issues.

Miriam is an excellent scientist. She had a successful graduate career, and her work in Steve's lab as a postdoctoral fellow in very interesting. Miriam has been interested in 3' end formation and termination, and made the unexpected discovery that Npl3, a protein implicated in mRNA transport, antagonized 3' end formation of mRNAs. Over the past 5 years, there has been a new paradigm linking numerous post-transcriptional events to the process of elongation, thereby permitting mRNAs to be treated differently (e.g. capped, spliced, polyadenylated) than other RNAs. Miriam's finding represents a new connection, and it is significant interest as evidenced by its publication in *EMBO J*. Miriam's continuing genetic analysis is being combined with biochemistry and array methodology, and I have little doubt that she will uncover new information on a very interesting subject. In this sense, she is well poised for a career as an independent investigator.

Miriam is very ambitious and wants to succeed. Aside from doing the science itself, she is always asking for scientific advice, comments on her ideas, and how to develop her career. This strong drive augurs well for the future, and I don't often see such a drive in her postdoctoral cohorts. She can function independently, and indeed the project she is working on is hers; she started working on this in Fred Winston's lab, and has continued it on her own. I don't have any information about her teaching abilities, but she is very organized and professional. While I would not rate Miriam among the very best postdoctoral fellows I have seen over the past 25 years at Harvard Medical School, she ranks well and is someone you should consider.

Sincerely yours,

Kevin Struhl

# Bristol-Myers Squibb Pharmaceutical Research Institute

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

October 13, 2005

Dear Dr. Brun,

It is a pleasure to write a letter of recommendation on behalf of Miriam Bucheli for a faculty position at Indiana University. While I was a faculty member at Rutgers University, Dr. Bucheli joined my laboratory as a Ph.D. candidate in February, 1998. Upon returning to research after taking time off to raise a family, she progressed well on her research investigating the role of Rad26p in nucleotide excision repair. Dr. Bucheli is very motivated and received a National Institutes of Health Minority Predoctoral Fellowship which allowed her to pursue her graduate research, all the while raising a child essentially by herself. This research focused on a member of the Swi2/Snf2 family of DNA-dependent ATPases, the aforementioned Rad26. Deletion of the *RAD26* gene results in a deficiency in transcription-coupled repair (TCR), the preferential repair of the transcribed strands of expressed genes over the nontranscribed strands and the genome overall. Dr. Bucheli demonstrated that the deficiency in TCR in a *rad26* mutant is dependent on the carbon source, a novel finding. In addition, Dr. Bucheli overexpressed Rad26p in yeast and found that the timing of expression of Rad26p is critical to restore TCR to a *rad26* mutant, another novel finding. Dr. Bucheli identified genes that, when present in multiple copies, suppress the UV sensitivity of a *rad7rad26* mutant lacking global genomic repair and transcription-coupled repair (the *rad26* mutant itself is not UV sensitive). These preliminary results will enable us to determine what proteins act in the same pathway as Rad26p. She also isolated four clones from a yeast genomic library which restore TCR to the *rad7rad26* mutant. As these clones each contain several genes, we will determine which of the genes is restoring TCR to *rad26* mutants.

Dr. Bucheli's data lead us to suggest that Rad26p enables TCR by altering the chromatin structure in regions undergoing transcription, rather than recruiting repair proteins to the RNA polII stalled at DNA lesions. Dr. Bucheli published two manuscripts as a first author in the journals *Genetics* and *Molecular Microbiology*. She is also the second author on a publication in the *Proc. Natl. Acad. Sci. USA*. I think that Dr. Bucheli



is an assertive and hardworking researcher who completed her graduate research in a timely manner in 2002.

Dr. Bucheli has since gone on to a postdoctoral fellowship with Dr. Fred Winston and then Dr. Stephen Buratowski, both at Harvard. She recently published a very nice manuscript in *EMBO Journal*, further testimony to her scientific ability and persistence.

I cannot provide an evaluation of Dr. Bucheli's didactic ability as she was not obligated to teach any classes during her tenure in my laboratory. However, over the years she has expressed a desire to teach at the undergraduate level. Based on her presentations of her own research at scientific meetings, I can say that I would expect Dr. Bucheli to present a talk in a clear and concise manner.

Dr. Bucheli is an eager scientist who acquired those skills necessary for research in molecular biology. These skills should enable Dr. Bucheli to develop her own research in molecular biology. She strives to think independently and pursue an experimental approach beyond that which was expected of her. I think Dr. Bucheli has very good scientific abilities and I am confident that she will have a productive career in molecular biology.

Sincerely,

A handwritten signature in cursive script that reads "Kevin S. Sweder".

Kevin S. Sweder  
Principal Scientist



October 16, 2005

Dear Search Committee:

I am writing to strongly support the application of Miriam Bucheli for a faculty position in your department. My lab has monthly joint group meetings with the laboratories of Steve Buratowski, Kevin Struhl, and Fred Winston. I have had the opportunity to meet Miriam and learn about her work on mRNA processing from these meetings. In addition, I am a member of the Harvard Medical School post-doctoral affairs committee, which works toward creating a community for the large number of post-doctoral fellows here and also organizes workshops on career opportunities for them. Miriam is one of the 3 post-doc representatives on the committee and has taken a leadership role in organizing workshops for our postdocs. So, I also know Miriam through working with her in this committee.

Miriam's research in the Buratowski lab has focused on mRNA 3' end processing. She carried out an elegant genetic screen isolating mutations that suppressed a defective termination signal in the GAL10 gene. This screen identified the elongation factors, Spt4 and Spt6, and the mRNA export protein Npl3 with roles in transcription termination. Miriam's subsequent experiments have established a role for Npl3 in the regulation of transcriptional termination and provide a link between mRNA export and 3' end processing. These results were recently published in EMBO journal and I am sure that Steve Buratowski will comment on them in more detail.

Miriam plans to continue the characterization of Npl3 and studies of mRNA 3' end processing in her own lab. I would like to state that I strongly believe that this is an extremely important area of investigation in the broad area of gene regulation. It has become clear over the past few years that mRNA processing, export, and stability are all directly coupled to transcription through the interaction of various factors with the RNA polymerase II itself. Furthermore, regulation of gene expression occurs at each of the above steps. Miriam's work will be at the interface between transcription termination, which involves interactions between RNA sequences, the polymerase, processing factors, and very likely the export machinery. Her work is therefore very likely to provide important new insights about the steps that regulate gene expression by controlling mRNA processing.

On a personal level, Miriam is one of the nicest people that I know. She is friendly and eager to talk about her science. Moreover, she is a caring member of the community

here, taking time from her work to improve the life of her fellow post-docs at Harvard medical School. Her leadership on the post-doctoral affairs committee here is an indication of the type of colleague that she is going to be: an outstanding department citizen.

In summary, Miriam is an excellent scientist with great potential for success as an independent investigator and teacher. She has my enthusiastic support.

Sincerely,

A handwritten signature in black ink, appearing to read 'DM', with a stylized, wavy line extending to the right.

Danesh Moazed  
Associate Professor of Cell Biology