DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY
HARVARD UNIVERSITY

16 Divinity Avenue
Cambridge, Massachusetts 02138

November 1, 2005

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

Dear Search Committee:

Adam Rudner was an excellent student who graduated from my lab in 2000. After an initial foray into mechanisms that held sister chromatids together, he settled on pursuing the observation that loss of Cdc55, a regulatory subunit of protein phosphatase 2A, inactivated the spindle checkpoint. His first experiments revealed that during mitosis, *cdc55*Δ mutants had more inhibitory tyrosine phosphorylation on Cdc28 (the budding yeast homolog of Cdk1/Cdc2) than wild type cells.

I was convinced that this observation told us that inhibitory phosphorylation of Cdc28 helped drive cells out of mitosis and urged Adam to design and execute experiments to test this idea. His analysis ended up convincingly showing that this hypothesis was utterly false. He developed the alternative hypothesis that the non-phosphorylatable mutants of Cdc28 that had been used in the initial experiments affected an activity of Cdc28 that was required for mitotic exit. Having provided strong support for this idea, Adam decided to test whether Cdc28 was responsible for phosphorylating and activating the anaphase promoting complex (APC), the key component responsible for the initiating anaphase. He showed that Cdc28 mutants reduced APC phosphorylation in vivo and that purified, recombinant Cdc28/cyclin B complexes could phosphorylate the APC in vitro. He then mutated all the potential Cdc28 phosphorylation sites in the three subunits of the APC that were phosphorylated by Cdc28, showed that this abolished their in vivo phosphorylation, and performed careful physiological analysis to show that the mutant cells had difficulty in activating the APC and triggering anaphase. Finally,, he provided evidence that the defect in the non-phosphorylatable mutants of Cdc28 was in the specific activity of individual protein molecules rather than the total cellular Cdc28 activity (number of molecules x specific activity) and provided a plausible model to explain how this defect might impair the ability of cells to initiate anaphase. This work appeared as a pair of papers in JCB.

I have described Adam's graduate work in some detail because it illustrates his strengths. Most prominently, it reveals his commitment to getting the right answer, however long it takes. In his case, doing so required extraordinary dedication, experimental skill, rigor, intelligence, and the

courage, patience, and stubbornness needed to show me that I was wrong. Perhaps the best tribute to the quality of Adam's work comes from my colleague David Morgan, an expert on protein kinases, with whom we had a joint group meeting. At the meeting where Adam showed the work the culminated his odyssey, David turned to me and said that Adam's data were among the most beautiful phosphorylation experiments that he had ever seen.

This well-deserved praise reflects Adam's drive to learn and improve. When he joined the lab, Adam's hands had trouble keeping up with his mind, and although he suggested many interesting experiments, their execution was often flawed. Because he analyzed his data rigorously, Adam was aware of this deficit and has worked tirelessly to eliminate it and hone himself into an outstanding experimentalist, skilled in genetics, cell biology, and biochemistry, who produces truly superior data.

For the last four years, Adam has been a post-doc with Danesh Moazed at Harvard Medical School. There, he has worked on the mechanisms that silence gene expression at certain chromosomal loci. His initial project was very ambitious, and aimed to reconstitute silent chromatin using purified components. Despite his best efforts, this proved impossible, and he moved on to the more tractable goal of carefully investigating the role of interactions between the Sir3 and Sir4 proteins that had been postulated to play a key role in silencing. His work confirmed that this interaction does occur and is required for efficient silencing. More recently, Adam has developed a method that gives a very clean, one-step purification of yeast chromatin and is using this to make an inventory of the proteins associated with silent chromatin, with a view to finding novel proteins and then using a combination of genetics, cell biology, and biochemistry to investigate their role in gene expression. The initial results have been promising, and he has one such candidate protein that he is currently investigating.

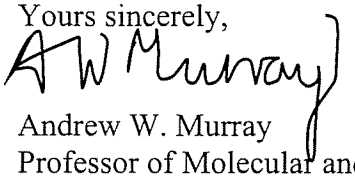
Adam has an exceptionally catholic and enquiring mind. He listens intently, rapidly grasps new material, and is always brimming with questions, interpretations, and suggestions for new experiments. He is a vital presence at both formal and informal discussions of science and has been a major contributor to the intellectual atmosphere of the lab. His enthusiasm and curiosity stimulated his colleagues in my and David Morgan's lab, and he often suggested critical experiments. I always enjoyed discussions with Adam and treated him as an intellectual equal from the day he started in the lab. He is uncompromisingly honest and insists on clear thinking and rigorous experimentation in his own work and that of others.

Adam's attention to detail means that he sometimes covers ground more slowly than others, and his desire to see the whole picture can lead him to concentrate on things that others would see as only marginally important. Both of these traits mean that he shouldn't compete in races in fashionable fields and that he may produce fewer papers than faster but less rigorous scientists, but they also mean that Adam's papers will all stand the test of time and that, more than once in his career, he will make a crucial observation that others, who passed more quickly, will have missed.

In summary, Adam has a rare enthusiasm for and intellectual commitment to science. His intelligence, commitment, honesty, and love of ideas will make him an excellent mentor. In his time with me and Moazed, he developed into an outstanding scientist who should become an

excellent PI. I would rank him in the top 10% of students that I have known, and expect that he will have a very productive career both as a researcher and a teacher. I recommend him very strongly.

Yours sincerely,



Andrew W. Murray
Professor of Molecular and Cellular Biology

UNIVERSITÉ DE GENÈVE

FACULTÉ DES SCIENCES
DÉPARTEMENT DE BIOLOGIE MOLECULAIRE
30, Quai Ernest-Ansermet -| CH-1211 Genève 4
Tél. +41 (0) 22 379 61 11 - Fax +41 (0) 22 379 68 68

David SHORE
Professeur

Ligne directe: +41 (0) 22 379 61 83
E-mail: david.shore@molbio.unige.ch

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

Genève, le 1 novembre, 2005

Dear Dr. Brun:

It is a great pleasure for me to write this recommendation on behalf of **Dr. Adam Rudner**, who is applying for a junior faculty position in your department. I have known Adam for over a year now, having worked closely with him during a sabbatical visit in Danesh Moazed's laboratory at Harvard Medical School in the second half of 2004. Before going into details, let me say first that Dr. Rudner is a truly outstanding young scientist who I am certain will become a successful and productive group leader and a wonderful colleague. I recommend him with the utmost enthusiasm.

To begin, I would like to emphasize that Dr. Rudner is certainly among the brightest and most talented postdoctoral fellows that I have ever come in contact with. I would compare him favorably to several individuals that I have known at a similar stage in their careers (for example at the LMB in Cambridge during the 1980s), all of whom are now successful faculty members at Harvard, MIT, UCSF, and elsewhere.

As an experimentalist, Dr. Rudner possesses a broad range of skills, is highly efficient, and remarkably meticulous. I have rarely encountered somebody with his depth of understanding of numerous techniques or his capability as a trouble-shooter. Adams's command of biochemical methods is remarkable (he is a genuine virtuoso biochemist), but he is also a very capable yeast geneticist. In short, his talents at the bench, and the intellectual foundation that underlies this expertise, are quite impressive. I was also able to see during my time in the Moazed lab that Adam is very hardworking and capable of sustaining a high level of output over extended periods of time.

Intellectually, Adam is clearly top-rate. His knowledge of the literature in the gene silencing field (as well as several other areas of molecular and cellular biology) is outstanding. His views of many problems are informed and sophisticated. He is highly critical but never dismissive, and has a keen sense for important details. Adam's ability to communicate his results and ideas, both verbally and in writing, is equally impressive. Without even the slightest hint of arrogance, he establishes himself as a major intellectual force in the lab, both at group meetings and during daily discussions with lab members. I very quickly began to regard him as an 'equal' colleague and have enjoyed numerous scientific discussions with him over the past year. (We're remained in close contact since my return to Geneva this past January). His ability to provide constructive criticism of other peoples' work is also exceptional. In short, Adam impresses me as somebody who is already operating at the level of a top-rate group leader / faculty member.

Adam takes a rigorous and thorough approach to problems and he is clearly committed to understanding detailed biochemical mechanisms in both the yeast silencing and cell cycle systems. This focus has led him to develop new techniques and a particularly fruitful collaboration with an outstanding mass spectrometrist, Scott Gerber, in the Gygi lab. In the past year or so Adam has established the groundwork for a new level of 'proteomic' analysis of native chromatin that I think will soon have a major impact. One can already see that his careful and elegant biochemical analysis has led to important insights into silencer function (Rudner et al., *MCB*, 2005). I am quite confident that his work in progress will be even more penetrating and groundbreaking. This is an ideal time for him to move on to an independent position, where he will soon establish himself as a key player in the field. I also think that the technologies he is developing will greatly benefit those around him who are shrewd enough to pick up on them. In this regard, I would note that Adam is very open and generous, and will gladly share his expertise with colleagues.

On a personal level, Adam is a joy to be around and somebody who naturally inspires excitement about science. He has a very positive attitude and I found that he was always willing to take the time to help others in the lab. It is rare to find somebody who is so intellectually and experimentally gifted, yet at the same time is able to interact so positively with everybody around him. For this reason (and many others), I am absolutely convinced that Adam will be a very successful group leader. I am also quite confident that he will be a wonderful colleague on may different levels.

In summary, I recommend Dr. Adam Rudner to you in the strongest possible terms. I think that he is an ideal candidate, in many different respects, who has great promise not only to do outstanding science, but also to effectively train young people and to participate actively in the intellectual life of a department. I would be delighted to have him here as a colleague, and I am certain that he will be highly appreciated by the department that is lucky enough to recruit him.

If you have any questions, or require any further information, please do not hesitate to contact me.

Sincerely,

David M. Shore, Ph.D.
Professor of Molecular Biology