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December 20, 2005

Dr. Yves Brun, Chair
Systems Biology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 East 3rd Street
Bloomington IN 4705-7005

Dear Members of the Search Committee:

I am writing to enthusiastically recommend **Dr. Elizabeth (Beth) Morin-Kensicki** for an Assistant Professor position in your department. I first met Beth in 2002 in my capacity as advisor to the UNC Office of Postdoctoral Services when she volunteered to serve on a committee evaluating our postdoc health insurance policy. Shortly thereafter we initiated a collaboration to examine the role of Yes-associated protein (YAP) in early embryonic development. We quickly realized how much we enjoyed working together, and after evaluating her progress since Terry Magnusson moved to UNC to become Director of the Center for Genome Science, Beth joined my lab approximately 2 years ago. I have thoroughly enjoyed watching Beth develop her own research projects in my lab and am confident that she has the intellectual ability, work ethic and drive needed to establish an independent research program. I am very impressed with Beth's ability to think creatively and to synthesize information quickly; after discussing broad concepts and goals with me, Beth deals with the experimental details, quickly sets up pilot studies, and begins collecting data.

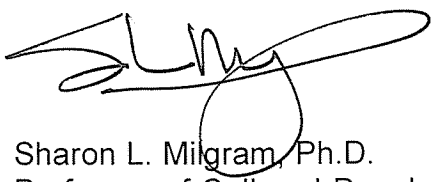
My lab studies the establishment of polarity and the organization of signaling scaffolds in neurons and epithelial cells. For a variety of reasons we became interested in the function of YAP, a protein first studied as a scaffold for the non-receptor tyrosine kinase c-Yes. To study the role of YAP in epithelial tissues, we decided to generate YAP knockout mice. To our surprise, the mice failed to develop beyond E8.5 and exhibited several distinct developmental defects. Since my lab has little experience with knockout mice and no experience in developmental biology, Beth has taken a leadership role in shaping all aspects of this project. She taught students and technicians in my lab how to dissect early embryos and has coordinated our efforts to understand the molecular basis

of the defects observed. Beth has patiently explained complex developmental processes and has generated many impressive figures for presentations and publications. She independently wrote the MCB manuscript describing our initial characterization of the mouse. One of the reviewers commented that the manuscript was beautifully written and that the quality of the data obviously represents painstaking attention to detail; another reviewer noted that the Discussion is superb. Beth was recently awarded a Scientist Development Grant from the National American Heart Association; after a few meetings to discuss general strategy, she developed and wrote the application with little input from me. In addition, Beth wrote a significant section of a recent NSF application on the role of YAP in gastrulation cell movements in *Xenopus* laevis embryos; although this application will not be funded this round, the reviews were generally positive and Beth has already developed a strategy for responding to the critiques when we resubmit in 2006. Beth understands how to write a grant; she pays careful attention to the details, but can also clearly articulate the "big picture". She is also aware of potential problems with the approaches she proposes and does an excellent job developing alternate strategies. Beth has outlined an ambitious plan for the future, including targeted gene deletions and the use of embryonic stem cells to probe the function of YAP. Beth recently initiated collaborative studies with an international lab to ask whether YAP and a closely related gene TAZ function coordinately during cellular differentiation. She is also learning many of the biochemical approaches commonly used in my lab to study protein interactions, and I believe Beth will successfully integrate these approaches into her research plan. I fully support Beth and intend to provide anything she needs to succeed (including mice, targeting constructs, antibodies, etc). Furthermore, my lab will not pursue additional developmental studies of YAP function once Beth starts her own research group.

Beth is a wonderful person to interact with; she is always available to answer questions and has established an excellent rapport with everyone in the lab. Beth goes out of her way to contribute to our research group and to the larger UNC community. For example, she recently worked extensively with a graduate student in my lab on his writing skills, taught a student in a neighboring lab how to isolate blastocysts, and volunteered to give a seminar to undergraduate students in our summer research program. This summer Beth provided our Postdoc Office with a copy of her AHA grant application and allowed us to "dissect" her grant in front of over 100 graduate students and postdocs. Beth has a great sense of humor and her energy and enthusiasm are infectious. Beth is very direct and candid; I enjoy debating science with her and look forward to our strategy meetings. Beth has gone out of her way to gain formal teaching experience. She developed, and twice taught, an undergraduate course in neuroscience and currently co-teaches a first year seminar for Ph.D. students in the Interdisciplinary Biomedical Science (IBMS) program. Beth is also gaining important mentoring and lab management skills. Last year she mentored one minority undergraduate student who is preparing for graduate school and she is working with three undergraduate students this semester. Beth is a dedicated mentor; she sets high standards, spends significant one-on-one time with each student, helps them prepare their presentations for lab meeting and undergraduate research symposia, and gives very direct feedback. The students have all requested to return to the lab next semester and they will continue working with Beth. After watching Beth interact with these and other students, I am confident that Beth will take her teaching and mentoring responsibilities very seriously.

Beth will make an excellent addition to your faculty and I encourage you to invite her to visit your department. Beth has the "right stuff" – a combination of tenacity, commitment, intellectual ability, and people skills that make me confident she will succeed. Beth needs to further strengthen her publication record and she is very aware of this. Several long-term projects in Terry Magnusson's did not come to fruition, but I believe Beth made the correct decision to change labs even though this somewhat slowed her progress. Beth and Terry have a cordial, but not warm, relationship and I do not fully understand why she did not thrive in his research group. Nonetheless, I am quite confident that Beth has the ability to run her own research group and that her work since joining my lab will establish her firmly as an excellent developmental biologist. Beth has traction in the lab – she now has the "floxed" YAP allele, has successfully derived a number of ES cell clones, and is close to another publication on apoptosis in YAP-null embryos. Beth is essentially running a small lab within my lab and is ready for the challenge of setting up her own research program. I know she will be an excellent colleague and that you will enjoy interacting with her. Please do not hesitate to contact me if I can provide additional information.

Sincerely,



Sharon L. Milgram, Ph.D.
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UNC
SCHOOL OF MEDICINE

Terry Magnuson, Ph.D.
Sarah Graham Kenan Professor
Chair, Department of Genetics
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CONFIDENTIAL

December 13, 2005

Dr. Yves Brun, Chair
Systems Biology Faculty Search
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RE: Elizabeth Morin-Kensicki

Dear Dr. Brun:

I am writing in support for Elizabeth (Beth) Morin-Kensicki's application for a faculty position within your department. Beth elected to come to my lab for postdoctoral work because of a keen interest in applying genetics and molecular biology to questions focused on mammalian development. She felt that insight into the genetic control of developmental processes is provided by phenotypic analysis of mutant embryos and my lab was using various genetic tools to produce these mutations. Beth first started on a project involving radiation to generate deletion mutations in mouse embryonic stem (ES) cells. A nested or overlapping array of deletions, an *in vivo* deletion complex, allows functional analysis of a specific chromosomal region. Coupling the deletions with an ENU mutagenesis protocol would allow the isolation of individual genes in the area that show a role in embryonic development. She began by preparing a vector containing the negatively selectable marker HSV-tk targeted for the NCAM region of the *Mus castaneous* chromosome 9 for electroporation into ES cells. In addition, to ease tracing an ENU mutagenized chromosome 9 through generations, she prepared a construct to create a line of mice carrying a dominant coat color marker targeted to the *Mus musculus 129/Sv Ncam* region. However, with the decision of the public and private genome projects to sequence the mouse genome, we made the strategic decision that functional analysis using deletion complexes was no longer required. Instead, if genes were going to be identified by computational methods, the best approach would be to go from gene sequence to mutation and to develop the ability to produce multiple mutations in any one gene. So, the lab successfully produced a mutagenesis scheme in ES cells for gene-based screens. Beth now has the ability to use this approach to produce mutations very rapidly in genes of interest.

While the above work was ongoing, Beth was pursuing other avenues of research. The prototype for applying ENU mutagenesis against a deletion complex to identify genes important for embryogenesis follows from the work of Rinchik and coworkers at the albino deletion complex on chromosome 7. An allele of the mouse polycomb group (Pc-G) gene, *eed* , was characterized in my lab. The *eed* mutation results in an altered fate map, disrupted anterior-posterior (AP) patterning in the primitive streak, and potential tissue-specific defects. To build upon these previous characterizations and define the role of *eed* in embryogenesis, Beth analyzed the expression patterns of a set of genes that initially "mark" tissue adjacent to the future anterior region of the embryo. Her results suggest that this

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early signaling pathway is intact in *eed* mutant embryos. She has now integrated this work with the zebrafish and amphibian model systems to synthesize a critical analysis of the influence of axis terminology on interpreting experimental results in a comparative manner across vertebrate models of development.

To gain in depth understanding of the *eed* homozygous phenotype, Beth turned to chimeras. Chimeric embryos comprised of wild type and mutant cells can reveal a great deal about the requirements of a gene for normal development. For example, cell/tissue interactions with a small number of wildtype cells may rescue largely mutant embryos or cell-autonomy of gene action may be revealed. Chimeras generated by injection of ES cells into blastocysts, give rise to embryos in which ES cell derivatives, identified by the constitutive expression of β galactosidase, may contribute in small or large part to the embryo as a whole. Using this approach, she was able to learn that the altered fate map observed for the *eed* mutant gastrula arises from cell non-autonomous actions of the mutated gene. These results reveal important information regarding our current model focusing on the lack of an anterior organizing center in the mutant embryo. Transplantation experiments will test this hypothesis and Beth has all of the tools to do these experiments. In summary, Beth combined molecular genetics to generate mutant embryos and a battery of tests designed to define resultant mutant phenotypes, which begins to address the genetic control of development.

Beth has a remarkable ability to synthesize information from the literature and to develop models to explain these concepts to others. Early events in development are complex and to make insightful hypotheses one must be able to integrate information from all embryological systems. Everyone in my lab, as well as others in the Department, have benefited from Beth's interpretation of their results. It is because she understands mouse embryology and can integrate the information with the zebra fish and amphibian literature. As a result, she is able to explain the significance of the observation in question. Also, Beth is a great writer and I can see her as an author of developmental biology textbooks.

Beth moved from my lab to Sharon Milgram's lab because the project that on which Sharon and I were collaborating began to take off and Beth was becoming the main driver of this project. Since this project originated from Sharon's lab, it made sense for Beth to move into the Milgram lab. I fully supported this transition and the work has now been published.

Sincerely,

T- Magnuson

Terry Magnuson, PhD