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AN HONORS UNIVERSITY IN MARYLAND

Department of Biological Sciences
University of Maryland, Baltimore County
1000 Hilltop Circle
Baltimore, Maryland 21250

PHONE: 410-455-2261
FAX: 410-455-3875
VOICE/TTY: 410-455-3233
www.umbc.edu

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

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Dear Dr. Brun,

I am writing to support Dr. Leonard R. Duncan in the strongest possible terms as a candidate for a tenure track position in your department. Len and I overlapped as postdoctoral fellows in the lab of Dr. David Kirk at Washington University during my last two years there, before I began my current position as Assistant Professor in the Department of Biological Sciences at the University of Maryland, Baltimore County. Despite the fact that Len left the Kirk lab to take a position at Cumbre in the spring of 2002 (because, unfortunately, his research efforts in the Kirk lab came to fruition just at the time funding for his work ran out), he and I have stayed in constant contact the past three-plus years to form what was first an "intellectual" collaboration that has grown into a very tangible and exciting one. As I describe in more detail below, Len has kept his *Volvox* research alive from a distance since leaving the Kirk lab, and is now poised to make extremely important contributions to the understanding of cellular differentiation mechanisms and their evolution.

Len arrived in the Kirk lab just at the time others succeeded in transposon tagging two of the most important developmental loci of *Volvox carteri*: *regA*, which is required for maintenance of the terminally differentiated state of somatic cells (one of two cell types in *Volvox*), and *glsA*, which is required for the asymmetric divisions that create progenitors of the second cell type, reproductive cells called gonidia. Len's plan was to use transposon tagging to clone one or more of the several known *lag* (for *late gonidia*) genes that repress somatic functions in the large cells created by asymmetric division, causing these large cells to differentiate (and remain as) somatic cells. Little did we know at that time that transposon tagging *V. carteri* genes is not very easy, at least using the transposons then available to us. Though he worked very carefully and doggedly, Len was not successful in cloning a *lag* gene, and abandoned those efforts after ~ two years. In fact, Len's transposon tagging experience was very similar to what others (including myself) have experienced since that time: despite ~15 postdoc-years of effort, only one additional *V. carteri* gene has been transposon tagged since Len joined the Kirk

lab, so I believe he was unwittingly facing long odds from the beginning with that project.

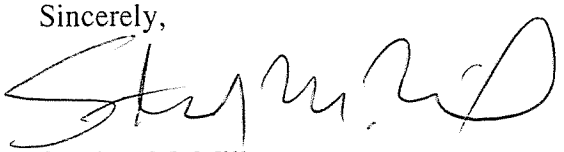
The above account is meant to explain how an extremely bright, creative, and perseverant scientist got off to a slow start in his postdoc, making it very difficult to establish a fundable research program in time to secure an academic position. Len made the most of a tough situation by regrouping and establishing new projects. First he cloned and characterized a new *Volvox* transposon (*Kangaroo*) that is now being used in transposon tagging experiments, and then he began his current line of research into the evolution of cellular diffentiation in *Volvox* by isolating an ortholog of the *regA* gene from *Volvox carteri* forma *kawasakiensis*, a taxon of *Volvox* closely related to the one in which almost all current studies are done. The point of this project was to identify conserved sequences that would provide clues into the function of the RegA protein, a putative transcription factor. Through this work Len discovered that *regA* is a fast-evolving gene that does encode one conserved domain, an ~100-aa domain distantly related to the DNA-binding SAND domain possessed by several plant and animal transcription factors. More interestingly, Len found that a gene (*rlsA*, for *regA-like sequence*) that encodes a very similar domain, which he named GARL (for Green Algal RegA-like) lies just upstream of *regA* in both *nagariensis* and *kawasakiensis*. The most exciting discovery of all was that Len found, upon inspection of the recently assembled *V. carteri* genome sequence, that it contains three additional GARL-domain encoding genes (*rlsB* and *rlsC*, just downstream of *regA*, and *rlsD*, which is unlinked). Furthermore, the genome of *Chlamydomonas reinhardtii*, the closest unicellular cousin of *V. carteri*, possesses a single GARL-domain gene that appears to be orthologous to *rlsD*. The stage is now set for some very intriguing studies into the functions of these *regA* homologs, which surely hold the key to understanding how cellular differentiation evolved in *Volvox*.

Len Duncan is one of the smartest people I have ever known. From my earliest interactions with Len in the Kirk lab and through my long-distance collaboration on some of his work on the evolution of cell differentiation, I have always been impressed by his ability to identify interesting questions, devise efficient strategies for approaching them, and rigorously carry them out. He is a very careful yet imaginative thinker who pays great attention to detail to make sure he always gets things right in the end (his *Genetics* paper on the *Kangaroo* transposon provides an excellent example of this). He is an extremely versatile scientist who already is exceptional with biochemical and molecular genetic methods and who can teach himself any technique or skill he needs to complete an investigation; around the time I left the Kirk lab he taught himself UNIX in part to simplify the task of assembling sequences he obtained from some large genomic clones of *Volvox* DNA. Len has a solid record of productivity overall, having publishing 10 high impact papers during his Ph.D. work with Richard Losick at Harvard. On the strength of his current research program, which will be enhanced by the goldmine of genome sequence data now available to him, there is no doubt that Len will be extremely productive as an independent investigator, and that he will be at the forefront of an intriguing and very fundable problem—determining how complex developmental traits like cellular differentiation evolve.

Len is exactly the sort of scientist and individual every biology department should have more of. He reads broadly and takes an active interest in the work done by those

around him, he has great ideas, and he is an excellent speaker and writer. He is also a team player who will do his share and more, without complaining, to make his department the best it can be. He is great with students and will be an excellent mentor to undergraduates and graduate students alike. And Len is truly an amiable and collegial person, always a pleasure to be around. In sum, Len is an excellent scientist and person who has a fantastic research program that is just waiting to take off. I give him my highest recommendation and urge you to bring him in for an interview to see for yourself.

Sincerely,



Stephen M. Miller
Assistant Professor
Department of Biological Sciences
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