

DEPARTMENT of CELL BIOLOGY
School of Medicine

December 29, 2003

Biocomplexity Faculty Search Committee
c/o Prof. Rob de Ruyter van Steveninck
Biocomplexity Institute
Indiana University
Swain Hall West 117
Bloomington, IN 47405-7105

Dear Search Committee Members:

It is a pleasure to write this letter of recommendation on behalf of **Dr. Lance Davidson**, who has applied for a junior faculty position in your Department. Lance joined my laboratory as a postdoctoral fellow in 1999 after initially coming to UVA with Ray Keller's lab following its move here from UC Berkeley in 1996. Dr. Keller and I both viewed Lance as someone who could serve as a vital collaborative link between our two laboratories. Lance has more than proved his worth in this regard and I consider him to be an outstanding colleague.

Lance proposed to follow-up on some intriguing observations from my lab and others regarding the likely cross-talk between integrin-ECM and cadherin based cell-cell adhesion at gastrulation in *Xenopus laevis*. This was the basis for his successful postdoctoral fellowship application to the American Cancer Society in 1999 in support of his studies in my laboratory. As a prelude to this line of investigation, Lance developed a novel explant system that will enable him to address the central hypothesis. The hypothesis is that cadherin and integrin functions are regulated reciprocally during development by both mechanical interactions with common cytoskeletal elements and through possible convergence of adhesion-dependent cell-signaling pathways. Lance plans to investigate this problem by using reagents that abrogate (or augment) the functions of either cadherins or integrins and to examine the effects on the remaining functional adhesive (i.e., cadherin or integrin based) system. The explant will make it possible for him to investigate the dynamic relocalization of critical cytoskeletal and signaling components that interact with cadherins and/or integrins. This will be done using GFP-fusions (e.g., FAK, paxillin, tensin, vinculin) and other fluorescently tagged molecules (e.g., tubulin, actin) that can be visualized by low-light timelapse digital and confocal imaging techniques.

I stress the details of his research plan because I think it is an exciting and very promising area of considerable importance – not only in the context of development but also in other situations where adhesive transitions are known to be of critical importance (e.g., epithelial-mesenchymal transitions important in wound healing and cancer and metastasis). In the course of developing his model system, Lance has also obtained some significant and fundamental new information regarding the importance of mesendoderm movements to gastrulation. This work highlights the roles of fibronectin/integrin interactions, not only in supporting the adhesion of these cells, but also in the regulation of mesendodermal mantle closure. Of interest was the unexpected discovery that the unique geometry of the blastocoel roof affects the mechanics of mesendoderm movements and the rate at which it closes. This is a particularly nice study published earlier this year Davidson et al., (2002). Given his accomplishments thus far, I believe Lance to be in a strong position to receive funding for his proposed research once he obtains an independent faculty position.

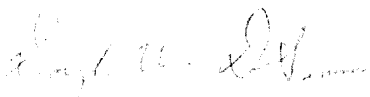
While Lance's intellectual contributions in lab have been substantial he has also driven technologies that have improved greatly our abilities to observe cells and their movements in vivo. Perhaps the best published example of this is a study on neurulation that Lance undertook in the Keller lab (Davidson et al., 1999: Development 126: 4547-4556). In this paper, Lance describes techniques that he developed for imaging embryos by confocal microscopy including fluorescent in situ hybridization. More recently, he has obtained some truly spectacular time lapse confocal images of fluorescently-tagged integrins and cytoskeletal elements that enable real time dynamic imaging of adhesive complexes in extending mesendoderm – a key “proof of concept” for much of his proposed research. Lance has excellent hands in lab and the considerable expertise in experimental embryology (the best I've seen!), optics and computing that are needed to push required imaging technologies ahead. While in my lab he added experience in molecular biology and some protein biochemistry. Needless to say, Lance is a very quick study and an impressive intellectual talent who is well aware of the important questions in morphogenesis and what it takes to do the “hard” experiment. I think he is clearly well equipped with the skills and talents needed to become a leader in development, morphogenesis and biomechanics, and these attributes will serve him well once he sets up his own research operation. He thinks deeply and very creatively about his science.

Lance has an unusual and varied background that includes training in biomechanics and molecular/cell biology as well as a strong footing in the physical sciences. This enables him to bring a refreshing perspective to biological research problems. In some ways, what has impressed me most about Lance has been his willingness to enter into free-wheeling discussions about how to define an important biological problem and, then, how best to approach it. These sessions are challenging, enjoyable, thought-provoking, and almost always lead to creative new ways at looking at old problems. I can think of no better compliment to attribute to a colleague and I believe you will find Lance to be an outstanding addition to your faculty for these reasons alone. I am quick to add, however, that Lance also “makes things happen” in lab and our discussions invariably go from the concept phase to experiment in short order. I easily rank Lance as one of the top 2 postdocs I have had in my laboratory in the past decade, and this company includes several outstanding individuals who have already gone on to their own faculty positions.

Finally, I have many reasons to believe that Lance will be an outstanding teacher and faculty colleague. First, he is an excellent speaker and very willing participant in both individual and group lab meetings. He has also given a number of talks at national meetings that have been well received. His presentations are very clear, well organized and lively. One on one, he is a patient and effective teacher who is willing to take the time to help fellow postdocs or students learn new techniques and/or understand difficult concepts. He doesn't shy away from difficult tasks, and while he remains focused on his own research interests, this does not come at the exclusion of more altruistic chores that do much to keep a lab running smoothly.

In conclusion, I think Lance is an outstanding individual who will bring to a faculty scientific excellence, novel perspectives and approaches to his research, and a high level of commitment and responsibility to his position. I am happy to recommend Dr. Davidson to you without reservation. Please do not hesitate to contact me if you require any additional information.

Sincerely,



Douglas W. DeSimone, Ph.D.

Professor