Harvard Medical School
DEPARTMENT OF GENETICS

77 Avenue Louis Pasteur
Boston, Massachusetts 02115
(617) 432-7871
(617) 432-7832 (FAX)

Dr. Jonathan G. Seidman
Henrietta B. and Frederick H. Bugher
Professor of Cardiovascular Genetics

December 17, 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

Re: Patrick Burgon, Ph.D.

Dear Members of the Search Committee,

We are pleased to support the application of Dr. Patrick Burgon for a position in the Biocomplexity Institute at Indiana University. Dr. Burgon is a talented young investigator with excellent teaching skills and a profound commitment to educational endeavors. Dr. Burgon joined our group in 2001, after the deaths of two mentors (Professor Ernest Peralta, Biological Laboratories, Harvard College and Professor Eva Neer, Brigham and Women's Hospital). Despite the considerable disruption to his training caused by these events, he has developed into a highly skilled bench researcher with a broad range of expertise in cell and molecular biologic techniques.

The focus of Dr. Burgon's research in our group has been to spearhead efforts to understand how human mutations in myosin binding protein C (MyBP-C) cause cardiac remodeling. His work focuses on a mouse model of human MyBP-C mutations that cause cardiac chamber enlargement and diminished ventricular function. Using immunohistochemistry and confocal microscopy he initially characterized the morphology of mutant MyBP-C myocytes and defined a previously unrecognized and intriguing structural abnormality. Although normal adult cardiac myocytes are binuclear, cells with MyBP-C mutations are predominantly mononuclear. Hypothesizing that binucleation reflected either enhanced cytokinesis or apoptosis late in development, he performed detailed analyses that excluded the apoptosis hypothesis. Experiments were then performed that indicate mutant myocytes have altered kinetics of cell division, exiting from the cell cycle later in the perinatal period than do normal myocytes. As a consequence, MyBP-C mutant hearts have myocyte hyperplasia. The importance of this study is broader than simply understanding the mechanisms by which these mutations could ventricular remodeling. A fundamental question in cardiac biology is why myocytes exit from the cell cycle. A long-

standing hypothesis has been that myofibrillar structure, which is to a large part orchestrated by MyBP-C, plays an important role in restricting cell division. Demonstration that myofibrillar structure directly attenuates division by Dr. Burgon may therefore have ramifications for pushing myocytes to re-enter the cell cycle.

Throughout Dr. Burgon's fellowship he has exhibited an extremely mature attitude regarding collaboration and teaching. Characterization of the MyBP-C mice has required interactions with a variety of outside investigators during the development of assays to study myocyte cycle kinetics, as these are not areas of expertise in the laboratory. Dr. Burgon showed considerable independence in identifying colleagues to help with techniques and experimental design. He works hard and is not daunted by tough experiments. In so doing, Dr. Burgon has had the opportunity to acquire and integrate a broad spectrum of research approaches including molecular imaging, genetics, molecular biology and biochemistry. These skills make him well positioned to initiate a comprehensive research program in a new environment.

Dr. Burgon is also a highly collaborative scientist. He has willingly devoted time and effort to teaching new techniques to others in our group. His particular attention to technical details has fostered the productivity of interactions on a number of different projects.

Unlike most fellows in our group, Dr. Burgon has also served as a member of the Board of Tutors at Harvard College for the past 4 years. He thoroughly enjoys teaching undergraduates, and enthusiastically invests the time and energy necessary to communicate complex ideas clearly. He has received high praise in this role at Harvard College. Not surprisingly these talents are reflected in his scientific presentations which are always well organized and scholarly.

In summary, we believe that Dr. Burgon is fully prepared to assume a position at Indiana University. Given his talents and motivation we are confident that he will continue to grow as a solid independent researcher. We recommend him to you with high enthusiasm and without reservation. If we can provide any further information, please do not hesitate to contact us.

Sincerely,

Jonathan Seidman, PhD
Professor of Genetics

Christine Seidman, MD
Professor of Medicine and Genetics