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Jeremy Bennett
Faculty Search Coordinator
Department of Biology
Indiana University
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Dear Dr. Bennett:

I am pleased to write in support of Dr. David Liu's application for a position in your Institution.

David is a highly talented investigator who entered my lab as a post-doctoral fellow in 1998 and who has risen to the rank of Associate Research Scientist.

The main direction of David's studies has been to determine at the molecular level how cell cycle molecules play a role in neuron cell death. This question is important not only because it provides fundamental information about neurons, but also because cell cycle molecules appear to participate in neuron death associated with a variety of neurodegenerative disorders. The first question that David tackled was to determine whether cell cycle dis-regulation in neurons leads to death by gene activation or via gene de-repression. In an elegant study published in *Neuron*, he was able to demonstrate that the key event is gene de-repression triggered by dissociation of E2F-Rb family complexes. In this study, he also suggested that among the key genes that undergo de-repression in neuron death is the transcription factor myb. Recently, in a paper published in *J. Neurosci.*, David was able to test this hypothesis and conclusively showed that de-repression of both c- and b-myb is required for neuron death resulting from trophic factor deprivation or DNA damage. In his current unpublished work (which will shortly be submitted), David has addressed the question of the identities of the E2F and Rb family members that regulate neuron survival and death and the manner by which they promote gene repression. His studies revealed that the main Rb family member associated with E2F in neurons is p130 (rather than Rb itself or p107) and that this forms complexes with E2F4 as well as the chromatin modifiers HDAC and Suv39H1 that repress genes such as mybs. Moreover, he demonstrated that such complexes are lost in response to

apoptotic stimuli via activation of cdk4 and that experimental interference with their formation or stability leads to neuron death. Finally, in collaboration with another lab member, David has recently discovered that one of the major downstream targets for b- and c-myb is the pro-apoptotic BH3-domain only molecule BIM. He has thus filled in a neuron cell death pathway starting with Cdk4 activation followed by loss of E2F4-p130-HDAC-Suv39H1 complexes, de-repression of b- and c-myb and consequent activation of Bim. This is a lovely body of work with important implications for preventing neuron death in a wide variety of clinically relevant conditions and has just been published in Genes & Development with another paper which has just appeared in J. Neuroscience.

Among David's strengths is his mastery of a broad range of experimental technologies in cell and molecular biology and his capacity to successfully add new skills to his repertoire as needed. He is quite independent in conceiving and implementing his experiments. He is hard working and well-organized and has been especially effective in identifying relevant findings outside neurobiology that are relevant to his studies of neuron death and differentiation.

On a personal level, David is well-spoken and has been a good collaborator both within and outside of the laboratory. Although he is not directly involved in classroom teaching, his presentations at lab meetings and conferences have been clear, well-organized and well-received. I have entrusted him to mentor several rotating graduate students and he has done an excellent and conscientious job in this regard. He has also been an active and valuable contributor to several invited reviews that we have co-authored.

In summary, David has shown himself to be a talented and productive investigator who is quite prepared for an independent position. I urge you to seriously consider his application.

Sincerely yours,

Lloyd A Greene

Lloyd A. Greene, Ph.D.
Professor of Pathology (in the Center
for Neurobiology and Behavior)