To members of the selection committee,

I am writing a strong letter of recommendation for Dr. Cuihong Jia for the MSU Postdoc Association Travel Fellowship to support her trip to the 10th International NPY-PYY-PP meeting. I have addressed the following requested points below.

a) Dr. Jia has made significant contributions to the project, which resulted in some very exciting findings that have broad applications across fields. She was given the task when she entered the lab to determine if a compound called NPY, released following injury simulation, induced progenitor cells to proliferate and begin to regenerate and replace the injured cells. She was able to confirm this hypothesis and then continued to independently expand on the topic by continuing to explore the molecular mechanisms of NPY-mediated proliferation. She demonstrated that the NPY Y1 receptor was involved and that the p44/42 ERK enzyme was involved. Thus, she successfully integrated her expertise from her graduate studies into my research to expand the scope of our research questions.

b) These results Dr. Jia will present are exciting because they identify a mechanism that both regulates stem cell self-renewal and maintains the population of neural stem cells throughout adulthood, something that is still not fully understood. We do know that neurotrophic factors like NPY produced by both neural and non-neural cells regulate neural stem cell proliferation and differentiation. However, the exact mechanisms underlying neurotrophic factor secretion are not known. This project shows that activation of the IP3R3 receptor mediates the release of the neurotrophic factor NPY in mouse olfactory epithelium. Furthermore, in the absence of the IP3R3 receptor, NPY release is diminished, and the number of basal cells, progenitor cells, and immature neurons is reduced. Under physiological conditions, this reduction in immature neurons and progenitor cells does not affect the rate of proliferation; however, following injury or damage, the regenerative, proliferative response is reduced and functional recovery is delayed. Addition of the neuroproliferative neurotrophic factor NPY to IP3R3<sup>−/−</sup> mice can restore the ability to proliferate. Thus, IP3R3<sup>−/−</sup> microvillous cells, via NPY release, have an important role in the maintenance of the neural stem cell population under normal conditions and following injury. This is the first report that definitively demonstrates a role for the microvillous cell.

c) These results identify microvillous cells and IP3R3 as new, innovative pharmacological targets to manipulate adult OE neuroregeneration. However, this research has applications to the central nervous system as well. Olfactory stem cells are a potential source for autologous stem cells to replace damaged neurons in neurological diseases. However, stem cell transplantation has substantial immunological, safety, logistical and economic hurdles. An alternative and perhaps complimentary therapeutic approach to transplantation could be the modulation of cellular and molecular regulators that normally control adult stem cell self-renewal, such as NPY and IP3R3 identified in this study.

d) It is important for Dr. Jia to attend this meeting because she is committed to studying NPY as an important regulator of neurogenesis. Her attendance to this meeting, her first NPY-specific meeting, will be beneficial to her as she begins to expand her own independent research interests. It will provide an opportunity to present her work in an oral presentation, which is an extremely valuable experience. Most importantly, she will meet new researchers and widen her network.

e) Dr. Jia is an outstanding young scientist and is an excellent candidate for this travel award. Since joining my lab, she has been very productive as evidenced by the eight papers on which she is an author, six on which she is the first author, and one in which she is a corresponding author. Dr. Jia is very independent, highly motivated, well read, and is always thinking about science. She is inquisitive and always asks intuitive and important questions at scientific conferences. In short, I believe that Cuihong possesses all the necessary skills, qualifications and personal qualities required to succeed as a well-funded, independent researcher.

Colleen Cosgrove Hegg, Ph.D.