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DEPARTMENT OF MOLECULAR & MEDICAL PHARMACOLOGY

February 8, 2004

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Dear Reviewers:

I would like to offer my strong endorsement for Mr. [redacted] application for Department of Defense Postdoctoral Fellowship Program.

Mr. [redacted] is currently a Ph.D candidate in Dr. Nelson at The Prostate Center, University of British Columbia, and he will join my research group at UCLA School of Medicine in July, 2004. I was very impressed about his work on the functional localization and competition between the androgen receptor and T-cell factor for nuclear β -catenin ([redacted] et al., *Oncogene*, 22: 5602-5613, 2003), and thought that his work is one of the most creative and thorough studies regarding β -catenin and hormone refractory prostate cancer in the current literature. I was, however, rather hesitate when he first approached me concerning postdoctoral research in my laboratory. I tried to dissuade him, using arguments concerning the desirability of moving into a different field and environment for one's postdoctoral research. [redacted] convinced me that he really wanted to work in what for him would be a new area – using molecular genetic approach and animal models to address one of the very difficult problems in prostate cancer research: the mechanism of hormone refractory prostate cancer.

It was during his interview and discussion of the possible projects with him, I realized how bright and creative he is. One of the major focuses of my research lab is prostate cancer biology. We have generated *Pten* prostate-specific knockout mice and showed that the *Pten* prostate cancer model recapitulates the disease progression seen in humans: initiation of prostate cancer with prostatic intraepithelial neoplasia (PIN), followed by progression to invasive adenocarcinoma, and subsequent metastasis with defined kinetics. Furthermore, while *Pten* null prostate cancers regress after androgen ablation, they are capable of proliferating in the absence of androgen. Global assessment of molecular changes caused by homozygous *Pten* deletion identified key genes known to be relevant to human prostate cancer, including those "signature" genes associated with human cancer metastasis ([redacted] et al. *Cancer Cell*, 4: 209-221, 2003). [redacted] pointed out that the key issue remain to be answered is the signaling pathway leading to androgen-independent growth of *Pten* null cells. He then proposed to directly assess β -catenin status and to further dissect the role of β -catenin nuclear localization and activation in tumor progression, especially in animals after hormone ablation therapy in vivo. I consider his approach penetrating, original, and experimentally feasible.