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Prof. Dimas T. Covas Professor Titular, Faculdade de Medicina de Ribeirão Preto Hemocentro de Ribeirão Preto University of São Paulo (USP) Ribeirão Preto, São Paulo, Brazil

Indianapolis, January 19th, 2012

Ref: Center for Cell Based Therapy-CEPID 2011

Dear Prof. Dimas Covas,

This letter is to express my enthusiastic support for your application to the FAPESP-CEPID Program to sponsor the "Center for Cell-based Therapy" (CTC) at Ribeirão Preto. I had opportunity to visit the Center, and was very impressed with the quality and scope of the research being developed by the different groups, and the state-of-the-art facilities and resources. The success of the Center and track record of publications illustrates the excellence of the investigators and their groups, and attest of the outstanding work of the Center's leadership in establishing and nurturing an environment of scientific excellence and competitiveness. In international conferences, I have had the opportunity to appreciate new work developed in the Center, namely last month at the Annual Meeting of the American Society of Hematology, in San Diego, CA. In addition to the intense research activity, the Center develops an important work in the training of young investigators (one of whom I had the privilege to host in my laboratory), and I was inspired by its important mission of providing expert medical service and scientific education to the community.

As you are aware, my group is interested in defining how oncogenic-triggered signals and microenvironmental cues are integrated within tumor cells, and contribute to tumorigenesis, tumor progression and drug-resistance. As part of this work we are interested in dissecting the mechanisms that regulate the tumor niche in the leukemic bone marrow BM, with particular emphasis on the role of the endothelium as a supportive niche for lymphoid leukemia cells and leukemia stem cells. Therefore, we are very interested in your work on the role of the endothelium in cancer biology, and on your fascinating research on endothelial-to-mesenchymal transition, and its impact in tumor progression and metastasization. Furthermore, we are excited with our ongoing collaboration with your colleague Dr. Aparecida Fontes, with two manuscripts now in preparation on the role of pericytes and mesenchymal cells on tumor progression. Also, I will be glad to participate in the interesting proposal by Dr. Fontes on the involvement of IncRNAs and chromatin modifiers in the deregulation of HOX genes, and their impact in the biology of medulloblastoma. This project is innovative and significant for this malignancy and for cancer research in general, since little is known on the epigenetic mechanisms controlling Hox genes in cancer, and there is a clear need for more effective molecular-targeted therapies for medulloblastoma.

In summary, I am delighted to continue to work and share our expertise with investigators at the Center for Cell-based Therapy, and want to express my enthusiastic support for this application, which will permit the advancement of the important research and training work being performed at the Center. I believe that this support will contribute for multiple new and important findings, and will contribute to



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the establishment of the CTC as a world-class research institution in cancer research and pioneer center for the development and implementation of cellular-based therapies.

I thank you for the opportunity to participate in this project, and I wish you the best of success for the present application and for the CTC.

Sincerely Yours,

Angelo A. Cardoso, MD, PhD

Ass. Prof. Medicine, and Medical and Molecular Genetics

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