

January 17, 2012

Ref: Center for Cell Based Therapy-CEPID 2011

Dear Professor Dimas Covas,

I am writing to let you know I would be delighted to collaborate with you on your CEPID 2011 project entitled: "Center for Cell Based Therapy"

The focus of my research has been to investigate the biological properties and regenerative capabilities of bone marrow-derived stem cells, in vitro and in vivo, to develop novel approaches to cell therapy and tissue repair. While significant advances have been made in the field of stem cell therapy, the spawned knowledge is still nothing but a very small tip of what is necessary to harness the true potential of stem cells and its application to the treatment of specific diseases. We used sheep as a large animal to test the engraftment and differentiative potential of putative HSC phenotypes and developed methods to expand and increase human HSC and MSC engraftment. Having demonstrated that transplantation of both unmanipulated and transduced human MSC and HSC results in robust widespread engraftment and long-term transgene expression, we re-established a line of sheep with severe hemophilia A (HA) in which new cell therapies can be tested. HA sheep have <1%FVIII, display multiple episodes of severe spontaneous bleeding including hemarthroses, muscle hematomas, and hematuria, all of which respond to human FVIII. These animals develop antibodies upon administration of human FVIII. We have recently demonstrated that paternal MSC transduced with a porcine FVIII-encoding lentivector and transplanted via the intraperitoneal route without preconditioning in hemophiliac lambs resolved the existent hemarthroses, and the spontaneous bleeds ceased.

Given my experience with the sheep model, stem cell biology and transplantation, I am ideally suited to collaborate in the proposed studies. I am particularly excited about your work, given the

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highly promising results you have thus far. I think our sheep model will be a great way to truly test the efficacy and safety of novel cell mediated therapies for Hemophilia A. I enjoyed my visit to Brasil last fall to discuss this project with you. Given our common interest and expertise, I am certain this will continue to be a fruitful collaboration.

I am delighted to work with you on this exciting project, and will be happy to help in any way I can.

Sincerely yours



Graça D. Almeida-Porada,MD,PhD
Professor of Regenerative Medicine
Wake Forest Institute for Regenerative Medicine
391 Technology Way
Winston-Salem, NC 27157-1083
Phone: (336)-713-1630

Wake Forest University School of Medicine