Preeclampsia Foundation 2008 Vision Grant

End-of-year report

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Project: *Potential Therapeutic Use of Relaxin in Preeclampsia*

The first aim of this project is to determine whether administration of relaxin to sFlt1-overexpressing gravid rats ameliorates disease symptoms in this model of preeclampsia. To that end, progress has been made in the production of the key reagents required to fulfill this aim. Specifically, the murine sFlt1 gene sequence was commercially synthesized and is currently being packaged into the AAV (serotype 8), in collaboration with William Hauswirth and the Viral Vector Core at the University of Florida. We anticipate successful generation of sFlt1-expressing AAV in the next few weeks, followed by propagation and purification. As explained in the mid-year report, we elected to switch from adenoviruses (as originally proposed) to AAV, because these viruses present a much lower safety hazard to laboratory personnel. In addition, we have access to novel AAV vectors with promoters that generate high expression levels of the transgene within 1 week, as required by our experimental design, as opposed to the typical time to peak expression for AAV of approximately 1-3 months.

We have also obtained the rat relaxin-neutralizing antibody (MCA1) required for these studies from the University of Illinois at Urbana-Champaign's Immunological Resource Center. The production of this reagent occurred over the second half of 2009 (a ~4-month process), and was underwritten by PE Foundation Vision Grant funds.

Once we have both reagents, we will commence studies on conscious, chronically-instrumented rats.

Hypothesis and Specific Aim 2 requires the use of subcutaneous arteries from normal and preeclamptic women, approval for the collection of which was granted in October '09 by the UF IRB. We anticipate beginning studies of isolated human arteries and successful completion of this aim in the coming months.

In summary, although the time-frame for the completion of this work has moved into 2010, we remain excited by the therapeutic potential of relaxin in preeclampsia and are grateful to the Preeclampsia Foundation for the opportunity to begin testing this idea in our models.

Sincerely,

Jonathan T. McGuane