

## James & Esther King Biomedical Research Program

***Perez-Pinzon, Miguel***

*Neurology  
University of Miami*

*2008 Program  
Bridge (1-year project)*

**Project Title:** Ischemic Preconditioning: Mechanisms of Neuroprotection

**Project Summary:** Multivariable assessment of stroke risk factors (e.g., Framingham, 15 Cardiovascular Health Study, 94 and the Honolulu Heart Study<sup>95</sup>) has identified cigarette smoking as a potent risk factor for ischemic stroke. Although the most effective preventive measures are never to smoke, quitting smoking is difficult. Thus, it is very important to define therapies that are efficacious against ischemic stroke in humans with non-preventable and preventable (smoking) risk factors.

Interestingly, the phenomenon of ischemic preconditioning has emerged as a potential therapy and was demonstrated to provide prophylactic protection in animal stroke models. [A prophylactic is a medication or a treatment designed and used to prevent a disease from occurring.] The most direct and significant application of understanding the mechanism of ischemic preconditioning is therapeutic access to this protective state in patients with high probability for a stroke, such as those that smoke or passive smokers. A major emphasis in this field is to understand the molecular mechanisms that mediate this phenomenon. In this context, a recent study from our laboratory demonstrated that the chemical resveratrol can emulate ischemic preconditioning neuroprotection against cerebral ischemia. Resveratrol, a phytoalexin found in red wine, is currently the focus of intense research both in the cardiovascular biology and in neurological sciences. We recently showed that a brief resveratrol pretreatment conferred neuroprotection against cerebral ischemia. The degree of neuroprotection induced by resveratrol was similar to that achieved by ischemic preconditioning. Based on our findings, we have proposed that resveratrol could be used as a prophylactic preconditioning agent. The translational value of resveratrol is supported by the fact that there are currently at least five clinical trials on resveratrol as an anti-carcinogenic compound. The main goals of the grant are to define the common signaling pathways activated by resveratrol and IPC that promote ischemic tolerance.