

## James & Esther King Biomedical Research Program

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Center for Aging & Brain Repair, Neurosurgery  
University of South Florida

2007 Program  
Bridge (1-year project)

**Project Title:** Splenic Mechanisms of Cord Blood Induced Brain Repair

**Project Summary:** Heart disease and stroke are the first and third leading cause of death and disability in the United States. Smoking has been implicated in approximately 1 in 5 deaths from cardio- or cerebro-vascular disease in this country while the death rate from stroke in Florida is the fifth highest in the nation. Clearly, tobacco places a significant burden on our healthcare system from these diseases alone. In a rat model of stroke (the middle cerebral artery occlusion or MCAO), we found that intravenously (i.v.) administering the mononuclear fraction from human umbilical cord blood (HUCB) enhances stroke recovery. Further, one of the biggest changes observed in the stroked brain after treatment with HUCB cells is a reduction in multiple indicators of inflammation. In addition, we observed changes in the T-cell population of the spleen after stroke; it returned to normal after HUCB transplantation. We hypothesized that the HUCB cells' ability to induce stroke recovery was critically dependent on the changes these cells induce in the spleen. This research project will explore the relationship between changes in pro- and anti-inflammatory cytokines in the spleen and behavioral and anatomical recovery from stroke. In Aim 1 we will examine this issue in animals in which the spleen has been removed and treated with or without iv HUCB cells. We will measure behavior, infarct volume (brain damage), astrocytes and microglia response to the stroke and cytokine production in spleen and brain. In Aim 2, we will determine which HUCB subpopulation alters spleen function using fluorescent-activated cell sorting (FACS) to isolate the individual HUCB subpopulations. These studies will increase our understanding of the critical role of the whole body immune response in the development of brain damage after stroke and the mechanisms underlying the recovery from stroke induced by HUCB cell transplantation. We may also identify other potential targets for development of stroke treatments that may extend the physician's arsenal in the battle against this devastating disease.