

James & Esther King Biomedical Research Program

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*Neurosurgery
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*2011 Program
New Investigator Research
(3-year project)*

Project Title: Hematopoietic [Animal] Stem Cell Function Following Acute Stroke Therapy

Project Summary: Smoking is a well-established, major risk factor for stroke. Smoking causes damage to brain blood vessels, leading to blockage in the arteries feeding the brain. This prevents fresh blood carrying oxygen and nutrients from reaching the brain. The only evidence based treatment for patients who have suffered a stroke is a drug given in the veins, which helps to dissolve the clot in the brain blood vessels (the “clot busting” drug, tPA). However, early research has suggested that, while clearly beneficial overall, tPA actually impairs the function of circulating stem cells in the blood, possibly limiting the ability for these cells to repair the injured brain. This investigation will seek to determine the mechanism by which tPA hurts stem cell function, as well as to determine if newer, promising applications of tPA directly at the clot site (with lower over amounts of tPA) will minimize some negative effects of tPA. A mouse model of stroke will be used to evaluate bone marrow stem cells and their subsequent entry into blood circulation in response to stroke. We will evaluate whether both routes of drug delivery produce viable, functional stem cells which enter the blood circulation. We will also evaluate the ability of the stem cells to enter blood vessels of the brain and repair the damage caused by the stroke. We predict that the intravenous route of drug administration may impair the functional ability of these stem cells to repair the damage.