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2001 Program
Investigator Initiated (2-year project)

Project Title: Cordblood cells treat stroke

Project Summary: The goal of this research project was to establish the efficacy of transplanting human umbilical cord blood (HUCB) cells as a treatment for stroke. The results demonstrated that HUCB produced significant, reproducible motor recovery when administered after stroke and may provide the basis for further development of a novel cell therapy approach to the treatment of this devastating disease.

Project Successes: There are a number of exciting outcomes of this research project. First, it was not necessary to pretreat the HUCB cells with agents that cause the cells to express neural proteins. Second, the HUCB cells produced better recovery when they were delivered intravenously than if they were transplanted directly into the brain. Third, it was determined that behavioral recovery occurred with 10^6 cells, but recovery was almost complete using 10^7 cells. At this latter dose, there was little anatomical damage observed 30 days after stroke and transplantation. Finally, after examining time points from 3 hours to 30 days post stroke, the optimal time to transplant the HUCB cells was determined to be 48 hours post-stroke. These results suggest that it will be possible to develop HUCB-based therapy for stroke that would be accessible to most stroke patients because it could be delivered non-invasively (intravenously) outside the current three hour therapeutic window, probably to patients with all forms of stroke.

Selected publications from BRP funded research in Peer Reviewed Journals:

Willing AE, Jiang L, Milliken M, Poulos S, Zigova T, Song S, Sanchez-Ramos J, Sanberg PR. Intravenous versus intrastriatal cord blood administration in a rodent model of stroke. *J Neurosci Res.* 2003;73:296-307.

Willing AE, Vendrame M, Mallery J, Cassady CJ, Hart CD, Sanchez-Ramos J, Sanberg PR. Mobilized peripheral blood cells administered intravenously produce functional recovery in stroke. *Cell Transplant.* 2003;12(4):449-454.

Vendrame M, Zigova T, Butler T, Pennypacker KR, Sanberg PR, **Willing AE**. A dose dependency study of human umbilical cord blood in a rodent model of stroke. *Stroke.* Aug 2004;10.1161/01.STR.0000141681.06735.9b. Print version Oct 2004.

Selected presentations from BRP funded research:

Lixian J, **Willing AE**, Poulos S, Sanchez-Ramos J, Zigova T, Song S, Chen J, Chopp M, Sanberg PR. Intravenous or intracranial transplantation of umbilical cord mononuclear cells reduces hyperactivity in a rodent model of stroke. American Society of Neural Transplantation and Repair. *Experimental Neurology.* 2001:170-218.

Sanberg PR, Chopp M, **Willing AE**, Zigova, T, Saporta S, Song S, Bickford P, Garbuzova-Davis S, Newman M, Cameron DF, Sanchez-Ramos J. Potential of umbilical cord blood cells for brain repair. International Society of Neurochemistry, *J Neurochem.* 2002;81(1):83.

Selected new grants based in part on BRP-funded work:

American Heart Association

Title: Modulation of stroke-induced inflammatory response after HUCB transplantation in the rat

Project period: 7/03 – 6/04

Award amount: \$120,000