

Prognosis of children with deadly inherited disorder may be improved by repeated hUCB injections

Tuesday 1 April 2014 - 1am PST

Source: Disclosure: AEW, SGD and PRS serve as consultants and founder, respectively, of Saneron CCEL Therapeutics, Inc., which provided the cord blood.

Citation: Willing, A. E.; Garbuzova-Davis, S. N.; Zayko, O.; Derasari, H. M.; Rawls, A. E.; James, C. R.; Mervis, R. F.; Sanberg, C. D.; Kuzmin-Nichols, N.; Sanberg, P. R.* [Repeated Administrations of Human Umbilical Cord Blood Cells Improve Disease Outcomes in a Mouse Model of Sanfilippo Syndrome Type III B](#). *Cell Transplant*. Appeared or available online: December 30, 2013 doi.10.3727/096368913X676916

New insight has been gained into treating an inherited disorder that creates serious neurological and behavioral disabilities in children and usually leads to death in the teen years.

In a recent study into the effects of human umbilical cord blood mononuclear cells (hUCB MNCs) when they are injected to counter the symptoms and progression of Sanfilippo syndrome type III B (MPS III B), researchers found that repeated injections into laboratory mice modeled with the disorder had clear benefits for the mice receiving multiple injections over control groups that received single injections of either a high or low dose of cells.

The study will be published in a future issue of *Cell Transplantation* but is currently freely available on-line as an unedited early e-pub.*

MPS III B results from a genetically programmed deficit of the Naglu enzyme. The deficit creates a build-up of heparan sulfate - a complex **carbohydrate** - that accumulates in lysosomes, cells that are responsible for waste disposal. With MPS III B, accumulations of heparin sulfate in the tissues are not eliminated and the accumulation causes damage to multiple organs, including the brain.

"Cell therapy has recently received attention as a potential treatment for lysosomal storage diseases," said study lead author Dr. Allison E. Willing, of the Center of Excellence for Aging and Brain Repair in the Morsani College of Medicine at the University of South Florida. "We have previously shown that a single hUCB injection into the cerebral ventricle of pre-symptomatic mice, or intravenous cell delivery at different disease stages, had a beneficial effect on the enzyme deficient mice. In the current study, we examined whether administering repeated doses of hUCB MNCs would have a greater effect than a single dose and help to prevent progressive neurodegeneration."

Using three groups of mice modeled with Naglu deficiency by knocking out the Naglu enzyme, the researchers injected one group with repeated doses of hUCB MNCs over a six month period. They

administered single doses - either high or low doses - to two other groups of similarly modeled mice. The group that had repeated hUCB MNC doses demonstrated a variety of favorable benefits.

To determine the benefits of repeated hUCB MNC injections, the researchers measured several behavioral and clinical outcomes before and after six months of treatment. These included **anxiety**, levels of heparin sulfate accumulation, and subsequent pathology in various anatomical brain locations.

"Repeated injections of hUCB MNCs produced the greatest neuroprotection," stated study co-lead author Dr. Svitlana Garbuzova-Davis, of the Center of Excellence for Aging and Brain Repair in the Morsani College of Medicine at the University of South Florida. "Hippocampal structural architecture remained intact in the repeated dose-treated mice as compared to the other groups. Also, there was restoration of the dendritic tree in the group receiving repeated doses. We also saw a striking reduction in microgliosis and microglial activation after hUCB MNC treatment."

The researchers speculated that administering hUCB MNCs may decrease **neuropathy** through modulation of inflammatory and immune processes as the hUCB MNCs produced numerous neurotrophic and growth factors.

"We demonstrated that hUCB MNCs were particularly effective at modulating anxiety in the Naglu knockout mice," concluded Paul R. Sanberg, distinguished professor at USF and principal investigator of the Children's Medical Research Foundation funded project. "Our results suggest that repeated administrations of hUCB MNCs produce greater amelioration of the underlying disease pathology. However, further studies will be necessary to determine if this treatment regimen can slow the progression of the disease, increase survival while minimizing symptoms, and determine whether improved outcomes are a function of enzyme administration, decreased **inflammation**, or both."

"This study highlights the benefits of using multiple injections rather than a single injection to treat Sanfilippo syndrome type III B" said Dr. John Sladek, Cell Transplantation section editor and professor of neurology and pediatrics at the University of Colorado School of Medicine. "This use of multiple treatments may be applicable to other neurodegenerative disorders, as already suggested by animal studies published by the same group for the treatment of **amyotrophic lateral sclerosis**."