Neural Stem Cells May Help Repair Spina Bifida in Utero

Pilot animal study shows promising results in the treatment of a this congenital defect before birth

(Vocus) September 9, 2008 -- A pilot animal study led by researchers from Children's Hospital Boston provides preliminary evidence that delivering neural stem cells (NSC) into the spinal cord, along with surgical coverage of the defect while in utero, may help repair spina bifida before birth. The delivered cells engrafted selectively in the most damaged areas of the spinal cord, remained viable, and produced neurotrophic and neuroprotective factors locally, the first steps in initiating a reparative process. The findings appear in the September issue of the journal, Surgery.

Spina bifida is a condition in which a portion of the spinal cord and its surrounding structures develop outside, instead of inside, the body. The defect develops at around the fourth week of gestation and can occur anywhere along the spine. Children with spina bifida suffer from partial paralysis, urinary and fecal incontinence, and musculoskeletal deformities. The condition has an overall mortality rate of 14 percent at 5 years.

Fetal surgery to repair this defect has been available for over a decade; however, the outcomes have shown limited improvement on spinal cord function. Only now is a large multicenter clinical trial comparing fetal repair to postnatal closure underway.

The Children's Hospital Boston researchers hypothesized that the surgery needs to be augmented by tissue regeneration techniques.

Dario Fauza, MD, of the Department of Surgery and Advanced Fetal Care Center at Children's, and colleagues studied a model of spina bifida in fetal lambs, involving a severe form of the condition known as myelomeningocele, in which a fluid-filled sac containing the spinal cord and nerves is visible outside of the back. Hoping to reverse a portion of the spinal cord damage, they used NSCs, which have previously been shown to mediate repair in a number of central nervous system abnormalities. To maximize the cells' regenerative impact, researchers administered the NSCs at 97-112 days of gestation (full term being 145 days) during the development of the spinal cord, rather than operating later in the more mature fetal stages. "To date, all that has been attempted is the prevention of further insult to the cord, rather than repairing the damage that has already occurred in utero," notes Fauza.

The Children's researchers, along with colleagues from Harvard Medical School and the VA Boston Healthcare System divided the animals into three groups. Group I saw no repair; Group II received standard surgical repair, with the open neural tube being covered by skin; and Group III received the same repair, plus an injection of NSCs directly into the spinal cord.

Once the surgery was completed, researchers monitored the fetuses through the remainder of gestation. Upon the birth of the animals, two examiners performed a basic clinical evaluation to check motor and sensory skills. The

survival rate was significantly lower in Group I (44 percent) than in Groups II (86 percent) or III (89 percent). The incidence of partial paralysis was also significantly worse in Group I compared with Groups II and III.

Group III showed a slightly lower incidence of partial paralysis than Group II, but the difference did not reach statistical significance. "In this introductory study, our goal was to validate the model and therapeutic concept by documenting the NSC survival, engraftment and early phenotypical patterns," said Russell Jennings, MD, of the Department of Surgery and Advanced Fetal Care Center at Children's. "Furthur studies will look at different forms of NSCs and alternative delivery methods, and will also provide the longer-term data needed to get a better idea of how successful repair in utero will prove to be for humans."

Though this research is in the beginning stages, the initial findings, paired with the vast amount of information on the use of NSCs in other forms of spinal cord injury, support further investigation into this prenatal approach.

The study was supported by a grant from the former Harvard Center for Minimally Invasive Surgery and by the Kevin and Kate McCarey Fund for Surgical Research, at Children's Hospital Boston.

Children's Hospital Boston is home to the world's largest research enterprise based at a pediatric medical center, where its discoveries have benefited both children and adults since 1869. More than 500 scientists, including eight members of the National Academy of Sciences, 11 members of the Institute of Medicine and 12 members of the Howard Hughes Medical Institute comprise Children's research community. Founded as a 20-bed hospital for children, Children's Hospital Boston today is a 397-bed comprehensive center for pediatric and adolescent health care grounded in the values of excellence in patient care and sensitivity to the complex needs and diversity of children and families. Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about the hospital and its research visit: www.childrenshospital.org/newsroom.

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