Human umbilical cord blood cells improve neurobehavioral outcome in a rabbit model of cerebral palsy

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Cerebral palsy (CP) has significant impact on both patients and society. As there are no curative therapies for CP, stem cells have been proposed as a possible treatment. Human umbilical cord blood cells (HUCBC) containing stem and progenitor cells have been used to treat genetic brain diseases. Previously, HUCBC improved outcomes after hypoxic-ischemic injury in small animals. Clinical trials using HUCBC are underway for neonatal injury and CP. We tested HUCBC therapy in a rabbit model of CP following hypoxic-ischemic (H-I) injury. Following uterine ischemia at 70% gestation, we infused HUCBC in a randomized fashion to newborn rabbit kits after birth with either mild or severe neurobehavioral changes. Infusion of high dose HUCBC, 5x10^6 cells, dramatically altered the natural history of the injury alleviating the abnormal phenotype including posture, righting reflex, locomotion, tone, and dystonia. Half the high dose showed lesser but still significant improvement. The swimming test however showed that joint function did not restore to naïve control function in either group. Tracing HUCBCs with either MRI biomarkers or PCR for human DNA found little penetration of HUCBC in the newborn brain in the immediate newborn period, suggesting that the beneficial effects were not due to cellular integration or direct proliferative effects but rather to paracrine signaling. In a large animal model, HUCBC improves motor performance in a dose-dependent manner perhaps by improving compensatory repair processes.

Biography
Sidhartha Tan completed his MBBS from the All India Institute of Medical Sciences, India and is neonatologist and clinician scientist. He is Clinical Professor at Department of Pediatrics, NorthShore University Health System and University of Chicago, IL. He investigates mechanisms of injury that result in cerebral palsy and mental retardation. He has developed an animal model that mimics cerebral palsy, one of the few models of its kind. His research has been continuously funded by NIH since 1992, and is now focused on bringing cures developed in the laboratory to the clinical realm to be used in human mothers and babies.

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