U of M sets course for cure of fatal childhood skin disease

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Physicians at the University of Minnesota and University of Minnesota Children's Hospital, Fairview have set the path to a cure for a young boy's fatal genetic skin disease, recessive dystrophic epidermolysis bullosa (RDEB), by using a cord blood and bone marrow transplant. Nate Liao, a 25-month-old from Clarksburg, N.J., underwent the experimental therapy in October 2007.

"We have established a new standard of care for these EB patients, beginning with Nate," said John Wagner, M.D., the lead University of Minnesota Medical School physician who developed the clinical trial. "Nate's quality of life is forever changed."

Because they lack collagen type VII, children with RDEB have skin that is exquisitely delicate. The skin and lining of their gastrointestinal (GI) tract is fragile; tearing and blistering occur with minimal friction. Coughing and vomiting often result in tears in the lining of the esophagus and stomach. Those affected must have their entire body continuously wrapped in bandages. Those who do not succumb from malnutrition and infection in childhood will acquire a uniformly fatal, aggressive cancer of the skin in young adulthood.

In collaboration with Angela M. Christiano, Ph.D., professor of dermatology and genetics and development at Columbia University Medical Center (New York, N.Y.), and investigators at Asahikawa Medical College (Asahikawa, Japan), and Jefferson Medical College (Philadelphia, Penn.), University of Minnesota researchers, Jakub Tolar,

M.D., Ph.D., and Bruce Blazar, M.D., discovered that certain stem cells found in bone marrow could correct the biochemical defect in RDEB in a mouse model of the disease. Marrow-derived stem cells greatly lengthened the life expectancy of the mice and healed existing blisters. Further testing by Columbia demonstrated that for the first time, these mice were producing collagen type VII and anchoring fibrils, the structures needed to bind skin to the body.

This is the first time physicians have approached the treatment of RDEB from a systemic perspective, using marrow-derived stem cells as a means to replace the missing protein, collagen type VII, throughout the body. Through the infusion of cells obtained from a healthy donor, the stem cells produce collagen type VII and correct the underlying genetic defect.

In October 2007, Nate Liao received marrow- and umbilical cord blood-derived stem cells and progenitor cells from his healthy, tissue-matched brother. Over the next six months, the skin and lining of his GI tract slowly improved, and skin biopsies on days 60, 130, and 200 documented increasing amounts of collagen type VII. By day 130, Nate's skin and the lining of his GI tract were beginning to show clinical signs that his skin was anchoring to his body.

Wagner and his team sought an external review of the skin biopsies. Photographs of the biopsies have been sent to dermatopathologists in London, England, and Portland, Ore., for independent analysis. Based on the success seen in Nate, Wagner will enroll additional RDEB patients into the clinical trial. Jacob Liao, Nate's brother who also has RDEB, received an unrelated donor cord blood transplant on May 30.

Source: University of Minnesota