NIH grant for the move toward clinical trials targeting the lysosomal storage disease MPSIIIB

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Investigators at Nationwide Children's have received a grant from the National Institutes of Health (NIH) to help move a therapy for MPS IIIB that has been shown effective in mice toward clinical trials in humans.

Mucopolysaccharidosis (MPS) IIIB, also known as Sanfilippo Syndrome B, is a lysososmal storage disease caused by deficiency in the essential enzyme NAGLU. Children with MPS IIIB appear normal at birth, but develop severe, progressive developmental delay and neurological disorders by 2 years of age. MPS IIIB is a fatal disease and there is currently no treatment available.

"To date, the greatest challenge in developing therapies for MPS IIIB has been the presence of the blood-brain barrier, which prevents therapeutics from entering the central nervous system," said Haiyan Fu, PhD, and the project's lead investigator.

For more than a decade, Dr. Fu's team in the Center for Gene Therapy in The Research Institute at Nationwide Children's Hospital has been focusing on developing gene delivery approaches to efficiently restore the central nervous system NAGLU activity, which is missing in MPS IIIB patients. Using a single intravenous injection of a recently characterized viral vector, AAV9, which has the unique ability to cross the blood-brain barrier, Dr. Fu's team has achieved the best long-term therapeutic benefits to date in adult MPS IIIB mice. This strategy has

resulted in correction of cognitive and motor function and extended survival in these mice, which like humans with MPS IIIB lack the NAGLU enzyme.

The NIH funding, awarded to Dr. Fu and co-investigator Kevin Flanigan, MD, will allow the team to complete necessary preclinical studies and to submit an investigational new drug application to the United States Food and Drug Administration for a Phase I/II AAV9 gene therapy clinical trial in patients with MPS IIIB. "Importantly, the intravenous rAAV9 gene delivery procedure is minimally invasive and is therefore a clinically relevant approach," said Dr. Fu.

"The Center for Gene Therapy at Nationwide Children's Hospital has been a leader in bridging gene therapy trials from the bench into the clinic, and we are excited about bringing that expertise to bear on this devastating disorder," added Dr. Flanigan.

Dr. Fu's MPS IIIB gene therapy project has received generous support since 2003 from the MPS III patient community through Ben's Dream – The Sanfilippo Research Foundation. A research grant from the foundation was critical in supporting Dr. Fu's team while they were pursuing the NIH grant application.

"We believe the quote that 'Hope sees the invisible, feels the intangible and achieves the impossible,'" said Jennifer Siedman, president and secretary of Ben's Dream the Sanfilippo Research Foundation. "Dr. Fu's recent research breakthrough and its recognition by the NIH with the awarding a U01 grant, brings to the Sanfilippo community the hope that a cure is on the horizon. The grant is not only a tribute to Dr. Fu's dedication to the field, but also to all the families and friends of Ben's Dream who have worked together for over a decade to fund this research."