Texas Children's NEUROSCIENCE NEWS

Texas Children's Hospital®

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Unique genetic mutation in California girl creates information sharing consortium

After visiting over 100 physicians across the country, the Wilsey family, based in San Francisco, could not determine what ailed their 3-year-old daughter, Grace. Her mysterious condition caused low muscle tone, lethargy, delayed cognitive and motor development, chalazion, alacrima, signs of liver damage and other severe health issues. Then they met Dr. Matthew Bainbridge of the Human Genome Sequencing Center at Baylor College of Medicine, the academic partner of Texas Children's Hospital.

Triggered by the realization that Grace could not produce tears, Bainbridge discovered a deficiency in her NGLY1 gene, which helps break down defective proteins so they can be reused throughout the body. Connecting with researchers at Duke University and the University of Utah, as well as several parents of children facing this genetic mutation, a network of knowledge and fellowship was formed. Using this new framework of information sharing, a consortium was forged bringing together clinical and non-clinical guidance to serve as an informal but invaluable resource for connecting and leading families and researchers towards solutions and answers.

"Having the support and engagement of the Wilsey family was critical to solving this case," said Bainbridge. "Their ongoing efforts in patient-research advocacy will be paramount to diagnosing and treating genetic diseases in the future."

These groups continue to discover more about this and other incredibly rare genetic mutations. Five treatment options are being explored on the 14 children worldwide with this disorder.

Interventional trial underway for Duchenne muscular dystrophy

Dr. Timothy Lotze, medical director for the Blue Bird Circle Muscular Dystrophy Association Clinic, is currently conducting a year-long interventional trial with PTC Therapeutics. The drug, ataluren, is a novel, orally administered small-molecule compound specifically constructed for the treatment of patients with disorders resulting from a nonsense genetic mutation, including Duchenne muscular dystrophy and cystic fibrosis.

These nonsense genetic mutations create premature stop signals in the translation of the genetic code contained in mRNA, which prevents the production of full-length, functional proteins. Ataluren interacts with ribosomes, cellular components that decode mRNA and manufacture proteins, allowing the ribosome to skip over the stop signal and produce a full-length, functional protein.

Texas Children's Hospital has three patients enrolled in the multi-center, double-blind study, which seeks to demonstrate drug safety and efficacy through partial restoration of patient muscle function. Data generated from this study may ultimately lead to FDA approval of ataluren as a treatment for Duchenne muscular dystrophy. As a hospital that provides care to approximately 150 boys each year with Duchenne muscular dystrophy, a disorder with no cure, this study represents an exciting step towards a potentially effective treatment.

Dr. Huda Zoghbi awarded prestigious 2014 March of Dimes Prize in Developmental Biology

Dr. Huda Zoghbi, founding director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital, will receive the 2014 March of Dimes Prize in Developmental Biology, an award given annually to investigators whose research has profoundly advanced the science that underlies the understanding of birth defects.

Zoghbi is best known for her pioneering work on Rett syndrome, a genetic neurological disease. Girls born with Rett syndrome develop normally for one or two years, but then begin to show progressive loss of motor skills, speech and other cognitive abilities. Males with the condition usually die in infancy.

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Zoghbi has been committed to searching for the genetic cause of the syndrome – a very challenging task – since she first encountered children with Rett syndrome in her residency. After a 16-year search, in 1999 she succeeded in identifying the Rett gene, a deficiency in a protein called MeCP2 which binds methylated DNA and regulates the expression of many other genes. This discovery consequently laid the groundwork for further studies by Zoghbi and other researchers and to the development of new therapeutic strategies currently undergoing clinical trials.

Texas Children's Hospital, located in the Texas Medical Center in Houston, is committed to creating a healthier future for children and women by leading in patient care, education and research.

We are proud to now operate under the official name of the **Neuroscience Center** at Texas Children's Hospital, bringing together the synergistic services of Neurology, Neurosurgery, as well as the Jan and Dan Duncan Neurological Research Institute (NRI).

Utilizing these teams, we are able to study, identify, monitor and surgically correct neurological conditions from the most simple to the most complex.

To learn more about neurological care at Texas Children's Hospital, please visit **texaschildrens.org/neuroscience**.

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