Researchers fight genetic killer of infants and toddlers

June 17 2010

Researchers at the University of Utah are making strides in understanding and combating a motor neuron disease known as Spinal Muscular Atrophy. The spinal muscular atrophies are a group of inherited diseases that cause progressive degeneration of motor nerves resulting in muscle weakness. The most common form of the disorder, due to the deletion of a critical gene on chromosome 5, is currently the leading cause of inherited infant and child mortality. Spinal Muscular Atrophy (SMA) is the second-most common autosomal-recessive inherited disorder after cystic fibrosis. Approximately 1 in 40 carry the gene for this disease.

With the generous support of Families of Spinal Muscular Atrophy, researchers in the University of Utah Department of Neurology are making significant headway in the fight against the disease. Once very poorly understood, SMA is now considered one of the genetic conditions closest to finding an effective treatment.

Kathryn J. Swoboda, MD, leads the team of University of Utah researchers investigating the disease and is the Principal Investigator for Project Cure SMA. "Families of SMA made an early and astute commitment to the development of a clinical trials network that has paved the way to bring new therapies rapidly to the clinic. Now, as several novel therapies approach clinical trials, we are well prepared to prove or disprove their efficacy. Without the tremendous support of Families of SMA over the past seven years, we would be unable to tackle the challenges that this disease presents to us as physicians, parents and

researchers. Families of SMA, from its modest beginnings more than 25 years ago, has served as a uniting force in the fight to improve the lives of every person affected by this disease."

Project Cure SMA is a clinical trials network of seven sites located in the United States and Canada, funded fully by Families of SMA. Their donations have included $2.75 million to the University of Utah team, along with more than $5 million in additional funding for other sites in the Project Cure SMA network. So far, the program has focused on testing existing drugs and validating outcome measures for use in future clinical trials that may lead to a treatment for Spinal Muscular Atrophy. Recently, an international expansion of these efforts has involved FSMA's international Partners in Argentina and Germany. Families of SMA has had the foresight and the courage to generously fund such work far in advance so that as novel drugs currently being designed for SMA become available, having a fully operational clinical network with a sufficient number of sites to conduct pivotal SMA drug trials will help attract and encourage biotech and pharmaceutical companies to invest in SMA drug development.

"We couldn't have accomplished what we have without the tremendous support of Families of SMA," notes Sandra P. Reyna, MD, Clinical Trials Manager for Project Cure SMA. "Their leadership has allowed us to develop a clinical trials network which will continue to pave the way for these efforts, and hopefully, encourage others to join us in developing the additional resources we will need to successfully support clinical trials for children and adults with SMA."

"Families of SMA initiated the Project Cure SMA Clinical Trials Network as a collaborative effort with leading SMA clinicians to achieve several goals for our community", said Jill Jarecki, PhD, FSMA Research Director. Establishing the network has provided us with the means to conduct natural history studies that increase our understanding

of disease progression, and to build models for designing SMA clinical trials that test the safety and efficacy of drug candidates in all SMA populations. Project Cure SMA has allowed us to build the needed infrastructure, including adequate regional clinical trial site representation across the US, for the testing of novel drug candidates while we have been conducting trials to test repurposed drugs for safety and efficacy in SMA patients. To date, the Project Cure Network has run 5 clinical trials testing repurposed drugs in all SMA patient populations".

The clinical spectrum of SMA ranges from early infant death to normal adult life with only mild weakness. However, the majority of those affected develop symptoms by the age of two years. Patients with SMA often require comprehensive medical care involving multiple disciplines, including neurology, pulmonology, orthopedic surgery, critical care, and physical medicine and rehabilitation; and physical therapy, occupational therapy, respiratory therapy, and clinical nutrition support. Genetic counseling is invaluable for the parents and family members who may also carry the gene. Intellect is normal and given the opportunity and support they need, they frequently thrive in the educational arena and successfully overcome their physical limitations to lead productive, vibrant lives.

Through the work of Dr. Swoboda and her colleagues in the University of Utah Departments of Neurology and Pediatrics, every child with SMA evaluated at the University of Utah's Clinical Neurosciences Center or at Primary Children's Medical Center (PCMC) is given the opportunity to enroll in the Project Cure SMA clinical trials. This allows the researchers to collect clinical information that can be used to advance their knowledge of the full spectrum of problems facing SMA patients and their families, whether or not these patients choose to enroll in the therapeutic clinical trials. These state of the art facilities and support of the University of Utah Center for Clinical and Translational

Science have been invaluable assets for supporting clinical research studies and trials for patients who travel here from Utah and around the country to consult with our team. Patients and families in turn benefit from the teams' experience and the series of specific protocols developed in Utah for optimizing clinical management of patients with SMA.

Committed to supporting research with the highest probability of advancing potential drug candidates, Families of SMA has forged collaborations with leading medical institutions and industrial partners in the United States and internationally. The funding of the Utah team is part of Families of SMA's broader strategy to integrate basic, translational and clinical research efforts into coordinated efforts aimed at facilitating drug discovery for the treatment of spinal muscular atrophy. Since its inception, the organization has funded more than $50 million in research initiatives, formed a number of collaborations with biotechnology companies, reduced barriers in the drug development process by providing open access to mouse models of SMA and has been instrumental in working with both Congress and the National Institutes of Health in creating awareness and increasing federal funding for the disease.

Provided by University of Utah Health Sciences