PEOPLE AGAINST LEIGH SYNDROME

April 20, 2016

The Honorable Harold Rogers
Chairman
House Appropriations Committee

The Honorable Nita Lowey
Ranking Minority Member
House Appropriations Committee

The Honorable Aderholt
Chairman
Subcommittee on Agriculture, Rural Development, FDA & Related Agencies
House Appropriations Committee

The Honorable Sam Farr
Ranking Minority Member
Subcommittee on Agriculture, Rural Development, FDA & Related Agencies
House Appropriations Committee

Dear Mr. Chairmen and Ranking Minority Members,

On behalf of patients and family members who have Leigh Syndrome, a rare mitochondrial diseases, I write today to share my concerns about draft language in the House FY2016 Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations bill. Contained within the legislation is Section 736, which would prohibit the United States from advancing critical research that would not only prevent mitochondrial diseases, but also hinder our country's position as a leader in the scientific sphere.

Mitochondrial diseases are devastating, inherited conditions that can lead to serious disability and death. They are passed from mothers to children and caused by defective mitochondria – the "batteries" that provide cells with energy. These diseases cannot usually be treated or prevented; however, we now have the science and technology to do just that.

Scientific advancements in reproductive in vitro fertilization techniques, known as mitochondrial replacement therapy (MRT), have ushered in a new era of medicine. This treatment will mean that parents with these defective genes will be able to have healthy children. American teams are developing this treatment, which has so far proven safe and effective in primates and un-implanted human embryos. Additionally, the Institute of Medicine thoroughly reviewed the social and ethical implications of this prospective treatment and concluded that it is ethically permissible to conduct clinical investigations of MRT within certain parameters.

Finally, the House prohibition language would allow other countries to move ahead, preventing our country from leading in mitochondrial research and disease prevention. More importantly, the House language would force parents in the United States facing these devastating diseases to leave the country in order to have healthy children or they will not be able to receive the treatment at all. Even worse,

many families will continue to have children suffering from these devastating diseases with many resulting in death. The United Kingdom, through the Nuffield Council, has already debated the social and ethical implications of the treatment, and the Parliament approved the ability to license these reproductive technologies earlier this year.

I would like to add a personal note; our family is a direct beneficiary for this type of research. Our seven year old son, Will, was diagnosed with Leigh syndrome five years ago. It was my egg, my mtDNA, which caused this mutation and devastating disease. My husband and I chose to end this disease in our family by not having any more biological children. To be given the option to have another child using our nuclear DNA is an unimaginable gift. One that we hope other families will be able to benefit from.

Without changing the language of this bill no family will have the chance to do so. Without changing the language of this bill, you are taking away important research which could change the lives of our families and most importantly the life of our son.

Every day we watch our son struggle to simply breathe; he is slowly dying and every day he's here is a gift, but it's a double edged sword. Every day he is still with us, his body is in pain. He will never run, ride a bike or enjoy some of life's most simple pleasures.

We have the opportunity to eradicate devastating mitochondrial diseases affecting one in 5000 children in the United States and continue to cultivate American innovation. I urge you and your colleagues to strike the rider language, in turn allowing mitochondrial disease research to advance. Thank you for your time and attention to this important matter.

Sincerely,

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PEOPLE AGAINST LEIGH SYNDROME
http://peopleagainstleighs.org/aboutleigh/

About Leigh Syndrome

Leigh syndrome is a progressive neurometabolic disorder with a general onset in infancy or childhood, often after a viral infection, but can also occur in teens and adults. It is characterized on MRI by visible necrotizing (dead or dying tissue) lesions on the brain, particularly in the midbrain and brainstem.

The prognosis for Leigh syndrome is poor. Depending on the defect, individuals typically live anywhere from a few years to the mid-teens. Those diagnosed with Leigh-like syndrome or who did not display symptoms until adulthood tend to live longer.

Long Name: Subacute Necrotizing Encephalomyelopathy.

Symptoms: Seizures, hypotonia, fatigue, nystagmus, poor reflexes, eating and swallowing difficulties, breathing problems, poor motor function, ataxia.

Causes: Pyruvate Dehydrogenase Deficiency, Complex I Deficiency, Complex II Deficiency, Complex IV/COX Deficiency, NARP.

The child often appears normal at birth but typically begins displaying symptoms within a few months to two years of age, although the timing may be much earlier or later. Initial symptoms can include the loss of basic skills such as sucking, head control, walking and talking. These may be accompanied by other problems such as irritability, loss of appetite, vomiting and seizures. There may be periods of sharp decline or temporary restoration of some functions. Eventually, the child may also have heart, kidney, vision, and breathing complications.

There is more than one defect that causes Leigh syndrome. According to Dr. David Thorburn, at least 26 defects have been identified. These include a pyruvate dehydrogenase (PDHC) deficiency, and respiratory chain enzyme defects – Complexes I, II, IV, and V. Depending on the defect, the mode of inheritance may be X-linked dominant (defect on the X chromosome and disease usually occurs in males only), autosomal recessive (inherited from genes from both mother and father), and maternal (from mother only). There may also be spontaneous cases which are not inherited at all.

One estimate of the incidence of Leigh syndrome (Leigh syndrome: Clinical Features and Biochemical and DNA Abnormalities by Dr. David Thorburn, PhD of Melbourne, Australia) is one in 77,000 births or one per 40,000 births for Leigh and Leigh-like disease (a milder version of the syndrome, often not proven by imaging or autopsy). However, this may be an underestimate since mitochondrial diseases tend to be under-diagnosed and misdiagnosed.

There is no cure for Leigh syndrome. Treatments generally involve variations of vitamin and supplement therapies, often in a “cocktail” combination, and are only partially effective. Various resource sites include the

possible usage of: thiamine, coenzyme Q10, riboflavin, biotin, creatine, succinate, and idebenone. Experimental drugs, such as dichloroacetate (DCA) are also being tried in some clinics. In some cases, a special diet may be ordered and must be monitored by a dietitian knowledgeable in metabolic disorders.

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Currently, there is a clinical drug trial underway for Leigh syndrome.
http://clinicaltrials.gov/ct2/show/NCT01721733?term=Leigh%27s+Disease&rank=1

The drug is showing promise and a new drug, EPI-589, also manufactured by Edison Pharma, is in progress.
http://edisonpharma.com/Home.asp

About Mitochondrial Disease

*Courtesy of the United Mitochondrial Disease Foundation:

Mitochondrial diseases result from failures of the mitochondria, specialized compartments present in every cell of the body except red blood cells. Mitochondria are responsible for creating more than 90% of the energy needed by the body to sustain life and support growth. When they fail, less and less energy is generated within the cell. Cell injury and even cell death follow. If this process is repeated throughout the body, whole systems begin to fail, and the life of the person in whom this is happening is severely compromised. The disease primarily affects children, but adult onset is becoming more and more common.

Diseases of the mitochondria appear to cause the most damage to cells of the brain, heart, liver, skeletal muscles, kidney and the endocrine and respiratory systems.

Depending on which cells are affected, symptoms may include loss of motor control, muscle weakness and pain, gastro-intestinal disorders and swallowing difficulties, poor growth, cardiac disease, liver disease, diabetes, respiratory complications, seizures, visual/hearing problems, lactic acidosis, developmental delays and susceptibility to infection.